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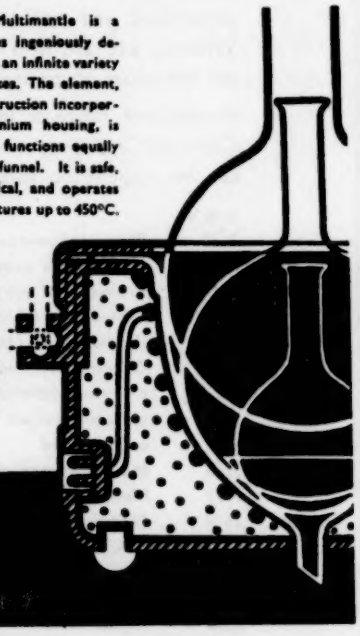

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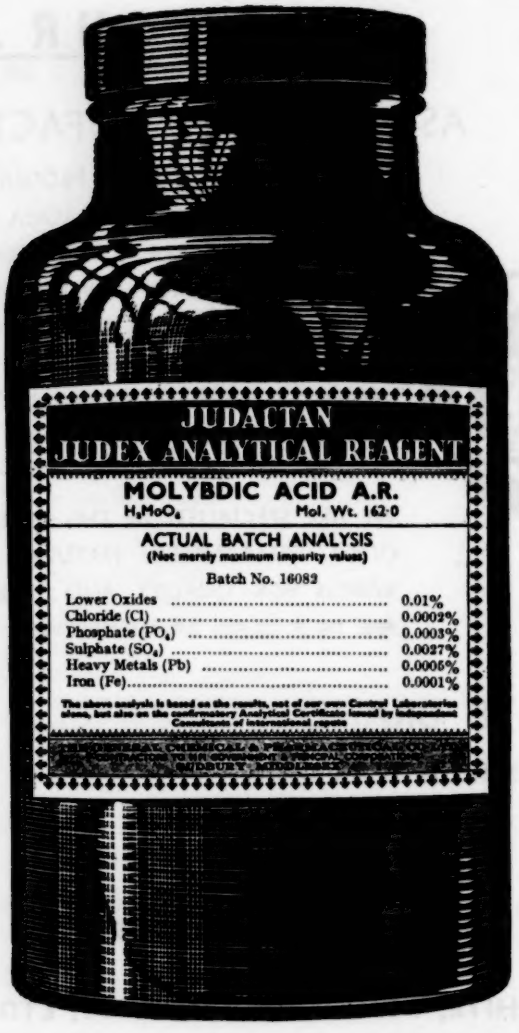
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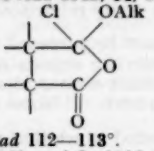
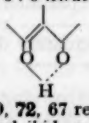
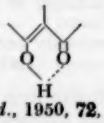
1947	1463	6	*for* 2 *read* 5.
1948	994	19	*for* 10^{-4} *read* IO_4^-.
	1719	20	for *Chem. Zentr.* read *Chem. Ztg.*
1949	1540	8 of text	*for* Montgomery *read* McDonald.
	3431	33	*for* 80 *read* 480.
1950	383	7 *	*for* $\varepsilon_{calc.} = 0{\cdot}87 \times 2 \times 10^{20}n = 1{\cdot}74 \times 10^{20}n$ *read* $\varepsilon_{calc.} = 0{\cdot}87 \times 2 \times 10^{20} \times 10^{-16}n = 1{\cdot}74 \times 10^{4}n$.
1951	1444	13 *	*for* 260 *read* 26.
	1449	1	,, ,,
	2344	Table I,	*for* R = NH_2 * *read* R = H*.
	3363	7	*for* Overend and Peacocke's *read* Gulland, Jordan, and Taylor's.
	3366	25	*for* method *read* workers.
	3367	Table I,	in legend, *for* * *read* †, *for* † *read* ‡, *and for* ‡ *read* *.
	3368	20	*for* (1 and 2) *read* (Figs. 1 and 2).
	3432	14	*for* OEt^b H *read* H OEt^b.
		16	*after* 1199 *insert* acetylated phenetole.
	3498	10 *	*for* 10 *read* 20.
1952	158	6 *	*for* (+)-*cis*-*p*-menth-2-ene *read* (+)-*p*-menth-3-ene.
	234	11 *	should read *Reactions with Thioglycollic Acid.*—(*a*) 2 : 5-Dihydrothiophen gave a *disulphide* (31%) as an orange, viscous oil, b. p. 175—180°/3 mm., n_D^{20} 1·5760 (Found : C, 39·9; H, 5·6; S, 36·7. $C_8H_{10}O_2S_2$ requires C, 40·4; H, 5·65; S, 36·0%). This afforded a *disulphone* as a benzene-.
	380	8	*delete* m. p. 28°.
	438	14	for (*Gazzetta*, 1943, **73**, 313) read (*Gazzetta*, 1939, **69**, 86).
	439	6	*for* 1941, **64**, 1696 *read* 1942, **64**, 1696.
	563	Formula (LX) should be	
	683	30	*for* 122—113° *read* 112—113°.
	813	7 *	for *loc. cit.*, p. 1120 read *J.*, 1936, 1120.
	1043	2	*for* α-picrototinic *read* α-picrotinic.
	1100	In Formula (XXI)	*insert* a 6-methyl group.
	1129	Fig.,	the legends for *A* and *B* should be transposed.
	1251	16 * (title),	for *Chloroundecafluorocyclohexanes* read *Perfluorinated Chlorocyclohexanes*.
	1368	Footnote,	*for* 1951 *read* 1952.
	1506	11	*for* 144° *read* 134°.
	1674	Table I,	for 2-Methyl-*n*-butyl fluoride, b. p./mm. should read 56·2°/757.
	1892	6	for *nitramides* read *nitramines*.
	2245	19 *	*for* cyclo*Hexene read* cyclo*Hexane*.
	2666	14 *	for 3 : 7-*Dimethyl*-9-(2 : 6 : 6-*Trimethyl*cyclo*hex*-1-*enyl*)-2 : 4 : 6 : 8-*tetraenoate* read 3 : 7-*Dimethyl*-9-(2 : 6 : 6-*Trimethyl*cyclo*hex*-1-*enyl*)-*nona*-2 : 4 : 6 : 8-*tetraenoate*.
	2762	Formula (XII).	*For*  *read* 
	2966	5 *	for *ibid.*, 1950, **72**, 67 read *ibid.*, 1950, **72**, 3030.
		last	for *loc. cit.* read *ibid.*, p. 67.
	2968	Legend to Fig. 3,	*for* 3·35 ± 0·05 × 10^{-6}M *read* 3·35 ± 0·05 × 10^{-5}M.
	3067	23 *	*for* 0·04 g. *read* 0·4 g.
	3723	Table I,	heading of eighth column, *after* Δλ *insert* Å.
	3725	Table II,	heading of seventh column, *after* Δλ *insert* Å.
	3782	9	for *Phenyl*-p-*tolylmethylphosphonic* read *Phenyldi*-p-*tolylmethylphosphonic*.
	4083	In Formula,	*for* CH_2:CR''·CH_2·O·CHR·CHR''·CHO *read* CH_2:CR''·CH_2·O·CHR·CHR'·CHO.

* From bottom of page.

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786. *Studies in the Polyene Series. Part XLIV.* The Preparation of Oct-4-ene-2 : 7-dione and Octa-3 : 5-diene-2 : 7-dione, Intermediates for the Synthesis of Carotenoids. The Anionotropic Rearrangement of Some Hexa-2 : 5-diene-1 : 4-diols.*

By R. Ahmad, F. Sondheimer, B. C. L. Weedon, and R. J. Woods.

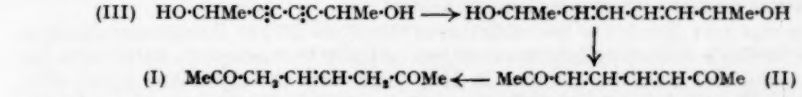
Routes to oct-4-ene-2 : 7-dione (I) and octa-3 : 5-diene-2 : 7-dione (II) from readily available materials have been developed. The diketone (II) is most conveniently prepared from octa-3 : 5-diyne-2 : 7-diol (III) by a two-stage process giving an overall yield of 40%.

Anionotropic rearrangement of the hexa-2 : 5-diene-1 : 4-diols (XII; R^1 = H, R^2 = Me and Pr^n; $R^1 = R^2$ = Me) gives mixtures of conjugated diene 1 : 2- and 1 : 6-glycols, the former predominating.

The investigations described in this paper were undertaken to develop routes to oct-4-ene-2 : 7-dione (I) and octa-3 : 5-diene-2 : 7-dione (II), neither of which had been described when this work was initiated. These diketones, possessing carbon skeletons identical with that of the central portion of β-carotene, offered promise as intermediates for the synthesis of various carotenoids. This view has recently been substantiated by the elegant syntheses from (I) of β-carotene, lycopene, and other polyene hydrocarbons by the Karrer and the Inhoffen school (Karrer and Eugster, *Helv. Chim. Acta*, 1950, **33**, 1172, 1952; 1951, **34**, 28, 1805; Karrer, Eugster, and Tobler, *ibid.*, 1950, **33**, 1349; Karrer, Eugster, and Faust, *ibid.*, 1951, **34**, 823; Inhoffen, Pommer, and Bohlmann, *Annalen*, 1950, **569**, 237; Inhoffen, Pommer, and Westphal, *ibid.*, 1950, **570**, 69; cf. Milas, Davis, Belič, and Fleš, *J. Amer. Chem. Soc.*, 1950, **72**, 4844).

Karrer and Eugster (*Helv. Chim. Acta*, 1949, **32**, 1934; cf. Karrer, Eugster, and Perl, *ibid.*, p. 1013) condensed glyoxal with acetoacetic acid to give (II), in ≯4% yields, and then reduced (II) to (I) with zinc and acetic acid in pyridine in 70—75% yield; conditions for the initial condensation were stated to be highly critical. This publication led two of us (Sondheimer and Weedon, *Nature*, 1950, **165**, 483) to give a preliminary account of the preparation of (I) and (II), in 15 and 2% yields, respectively, by the action of dimethylcadmium on the acid chlorides of dihydromuconic and muconic acids, the dihydromuconic acid being conveniently prepared from butadiene *via* 1 : 4-dibromo- and 1 : 4-dicyano-but-2-ene (see p. 4092).

Later Inhoffen, Pommer, Winkelmann, and Aldag (*Chem. Ber.*, 1951, **84**, 87) hydrogenated, by a poisoned palladium catalyst, the readily available diacetylenic glycol (III) (Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1579; Armitage, Jones, and Whiting, *J.*, 1951, 44) to a mixture which with *tert.*-butyl chromate (cf. Oppenauer, *Anal. Asoc. Quím. Argentina*, 1949, **37**, 246) gave (II) in 5% overall yield. The intermediate glycol (IV) was isolated as a crystalline solid, m. p. 100°, after regeneration from the dibenzoate, m. p. 140°.



The yields in all published methods for the preparation of (I) and (II) leave much to be desired, but a convenient method for the conversion of (III) into (II) in 40% overall yield has now been devised.

Reduction, with lithium aluminium hydride, of alcohols ≻C:C·C:C·C(OH)≺ to the corresponding diene alcohols (Chanley and Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4140; Raphael and Sondheimer, *J.*, 1950, 3185; Bharucha and Weedon, forthcoming publication) and of 2 : 7-dimethylocta-3 : 5-diyne-2 : 7-diol to the diene glycol (Professor E. R. H. Jones and Dr. M. C. Whiting, personal communication) suggested the use of this reagent. Treat-

* Part XLIII, *J.*, 1952, 2657.

ment of (III) with 1·3 mol. proportions of lithium aluminium hydride gave an oil (74%) which was estimated by light-absorption data to contain 64% of the required glycol (IV). By increasing the proportion of hydride to 3·5 mols., the purity of the product was raised to 83% but the yield was only 41%. Since the crude glycol can be oxidised to the diketone (II) almost quantitatively (see below), the former procedure is much preferred. After regeneration from its dibenzoate, m. p. 80°, the diunsaturated glycol (IV) was obtained as a solid of m. p. 45°. These melting points vary greatly from those of the products reported by Inhoffen *et al.*, a fact which may be ascribed to a difference in configuration about the double bonds. Whereas catalytic hydrogenation, employed by the German workers, would be expected to give mainly a *cis-cis*-diene (cf. Campbell and Campbell, *Chem. Reviews*, 1942, **31**, 148; Inhoffen, Bohlmann, Aldag, Bork, and Leibner, *Annalen*, 1951, **573**, 1; Bohlmann, *Chem. Ber.*, 1951, **84**, 545), reduction with lithium aluminium hydride probably gives the *trans-trans*-isomer since reduction of but-2-yn-1-ol with this reagent yields *trans*-crotyl alcohol (Bharucha and Weedon, *loc. cit.*).

Further support for the *trans-trans*-configuration of the glycol, m. p. 45°, comes from a consideration of its ultra-violet absorption properties and those of the *cis*- and the *trans*-form of hexa-3 : 5-dien-2-ol and piperylene (see Table 1). In piperylene no steric inhibition

TABLE 1.

	$\lambda_{max.}$, Å	$\epsilon_{max.}$		$\lambda_{max.}$, Å	$\epsilon_{max.}$
HO·CHMe·CH:CH·CH:CH·CHMe·OH	2270	32,000	CHMe:CH·CH:CH_2 (*trans*) [2]	2235	23,000
	2340 *	24,500	CHMe:CH·CH:CH_2 (*cis*) [2]	2230	22,600
HO·CHMe·CH:CH·CH:CH_2 (*trans*) [1] ...	2230	28,000	CHMe:CH·CH:CHMe [3] ...	2270	22,500
HO·CHMe·CH:CH·CH:CH_2 (*cis*) [2]	2240	20,000			

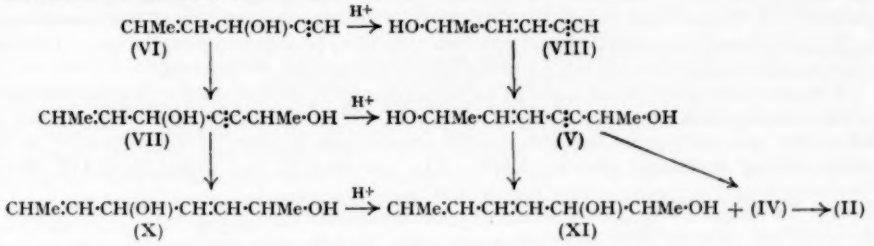
* Inflexion. [1] Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 88. [2] Braude and Coles, *J.*, 1951, 2085. [3] Booker, Evans, and Gillam, *J.*, 1940, 1453.

of coplanarity occurs in either the *cis*- or the *trans*-form, and the absorption of the two geometrical isomers is therefore identical. With the hexadienols, however, the intensity for the *cis*-form is reduced below that for piperylene and 1 : 4-dimethylbutadiene by steric interference between the CHMe·OH and the $CH:CH_2$ group (Braude and Coles, *J.*, 1951, 2085). A similar, or more pronounced, reduction would be expected with (IV) if this possessed a configuration other than *trans-trans*. The intensification which is actually observed with the glycol, m. p. 45°, may be attributed to the larger hyperconjugative properties of the C·OH compared with the C·H group, an effect noted previously with *trans*-hexa-3 : 5-dien-2-ol (*idem, loc. cit.*) and other ethylenic alcohols (Braude and Timmons, *J.*, 1950, 2000, 2007).

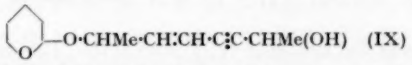
Independently of this work, the reduction with lithium aluminium hydride of (III), and other diacetylenic glycols, has been studied by the Manchester school (Bates, Jones, and Whiting, forthcoming publication). By using 4 mols. of hydride an oil was obtained in 45% yield which exhibited light-absorption properties similar to those observed in the present investigation for the 83%-pure diene glycol. The crystalline diene glycols obtained by similar reduction of some other diacetylenic glycols were shown by infra-red absorption measurements to possess a *trans-trans*-configuration.

Attention was next directed to the oxidation of the glycol (IV) to the required diketone (II). Of the methods studied by Inhoffen *et al.* (*loc. cit.*) only that using *tert.*-butyl chromate proved successful and gave the diketone in 13% yield from the crystalline glycol (IV), m. p. 100°. Oxidation of the glycol (IV), m. p. 45°, by shaking it with manganese dioxide in acetone (cf. Bharucha and Weedon, *loc. cit.*; Woods and Weedon, *J.*, 1951, 2687) gave the crystalline diketone (II) in 70% yield. A more valuable procedure, however, was oxidation of the crude reduction product of (III), containing *ca.* 64% of (IV), without isolation of the crystalline diene glycol. In this way (II) was obtained in 91% yield [based on the estimated content of (IV)], *i.e.*, in 35% overall yield from (III). Similar oxidation of the crude product formed by catalytic hydrogenation of (III) according to Inhoffen *et al.* (*loc. cit.*) gave (II) in 4% overall yield. Reduction of (II) by Karrer and Eugster's method (*loc. cit.*) gave crystalline (I) (80%) identical with that prepared from dihydromuconic acid.

The diketone (II) has also been prepared *via* the glycol (V). Reaction of the Grignard complex of the readily available hex-4-en-1-yn-3-ol (VI) (Heilbron, Jones, and Weedon, *J.*, 1945, 81) with acetaldehyde led to the glycol (VII) in 70% yield. This, on treatment with dilute sulphuric acid, underwent anionotropic rearrangement to (V) which was also obtained in 70% yield from hex-3-en-5-yn-2-ol (VIII) (Heilbron, Jones, Smith, and Weedon, *J.*, 1946, 54) and acetaldehyde.



Selective partial reduction of (V) to (IV) proved more difficult than that of (III). By both catalytic hydrogenation, a partly poisoned palladium catalyst being used, and reduction with lithium aluminium hydride, mixtures of glycols were formed which on oxidation (manganese dioxide) furnished the diketone (II) in 14 and 8% yields, respectively [based on (V)]. While (IX) on treatment with lithium aluminium hydride gave the corresponding



diene (73%), conversion of the latter into (II) could be accomplished in poor yield only.

The partial hydrogenation of (VII) to (X), and the anionotropic rearrangement of the latter, were also examined as a route to (IV). Although the partial reduction of acetylenic 1 : 4-glycols has been investigated extensively by Zal'kind and others (for review see Johnson, "Acetylenic Compounds," Vol. I, Ed. Arnold & Co., London, 1946), few examples containing an alkenyl substituent have previously been reported. As with (VI) and related compounds (Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 84), partial hydrogenation of the triple bond in (VII) proceeded smoothly, in ethyl acetate solution with a 0·3% palladium–calcium carbonate catalyst, to give (X) in 90% yield.

Anionotropic rearrangement of (X) occurred on treatment with 0·2% sulphuric acid for 1·5 hours giving, in almost quantitative yield, an oil which exhibited high-intensity light absorption in the 2230-Å region. The product, however, consisted of a mixture of the fully conjugated isomers (IV) and (XI), the latter predominating, which on oxidation (manganese dioxide) gave the diketone (II) in *ca.* 7% yield. Periodate oxidation of the mixture caused fission of the α-glycol to acetaldehyde and sorbaldehyde, the yield of the latter (as the semicarbazone) indicating that the initial mixture contained at least 50% of (XI). Catalytic hydrogenation of the rearranged glycols furnished a mixture of octane-2 : 7- and -2 : 3-diol, containing at least 60% of the former (periodate titration), which on oxidation with chromic acid yielded octane-2 : 7-dione (20%).

Under the conditions employed for the isomerisation of (X), conversion of the symmetrical glycol (IV) into the α-glycol (XI) occurred to only a small extent (<2%). The initial rearrangement of (X) therefore gives mainly (XI) rather than (IV) which would be the thermodynamically more stable product in view of the strong hyperconjugative effects of the C·OH groups. Isomerisation of (X) under more vigorous conditions was accompanied by extensive polymerisation but the composition of the resulting mixture of glycols showed no marked change.

Previous investigations of the rearrangement of unsymmetrical dialkenylcarbinols show that the hydroxyl group migrates initially to the γ-carbon atom at which electron accession is greatest (Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 84; Braude and Timmons, *J.*, 1950, 2007, Braude and Coles, *J.*, 1950, 2014). This principle seems inadequate, however, to account for the formation mainly of (XI) on isomerisation of (X), since the dissociation

constants of acetic acid ($1{\cdot}75 \times 10^{-5}$) and lactic acid ($1{\cdot}38 \times 10^{-4}$) indicate that the electron-releasing properties of the methyl group are greater than those of CHMe·OH. Furthermore electronic interaction (hyperconjugation) between the CHMe·OH group and the adjacent double bond would be expected to take place by way of contributions to the resonance hybrid of forms such as $-CH{:}CH{\cdot}\overset{+}{C}HMe\ \bar{O}H$ and $-\overset{+}{C}H{\cdot}CH{:}CHMe\ \bar{O}H$, which again would not favour α-glycol formation. A possible explanation is that a cyclic intermediate is involved (cf. Braude and Coles, *J.*, 1951, 2085); the *cis*-configuration of the double bond in (X) introduced by catalytic hydrogenation may then be a determining factor. This and other aspects of the reaction will be investigated as opportunity permits.

The novel formation of an α-glycol by isomerisation of an ethylenic 1 : 4-glycol has been further exemplified by rearrangement of (XII; $R^1 = R^2 = Me$) and (XII; $R^1 = H$, $R^2 = Pr^n$), prepared in 90 and 65% yields, respectively, by partial hydrogenation of the corresponding acetylenic glycols (XIII). The presence of the α-glycols (XIV) in the

$CHMe{:}CH{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}CR^1R^2{\cdot}OH$ (XII)

$CHMe{:}CH{\cdot}CH(OH){\cdot}C{\equiv}C{\cdot}CR^1R^2{\cdot}OH$ (XIII)

$CHMe{:}CH{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CR^1R^2{\cdot}OH$ (XIV)

rearranged products was established by treatment with periodate and isolation of sorbaldehyde. In the conversion of the acetylenic glycols into sorbaldehyde the isolation of the intermediates may be omitted. Thus sorbaldehyde (as the semicarbazone) was obtained from (XIII; $R^1 = R^2 = Me$) and (XIII; $R^1 = H$, $R^2 = Pr^n$) in 25 and 82% overall yields, respectively.

Other routes examined did not lead to (I) and (II). The acetylenic glycol (XV) was prepared from propylene oxide and the Grignard complex of both acetylene and pent-4-yn-2-ol and on catalytic hydrogenation gave (XVI). The latter could not, however, be oxidised to (I).

$C_2H_2 \longrightarrow HO{\cdot}CHMe{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CHMe{\cdot}OH$ (XV) $\longrightarrow HO{\cdot}CHMe{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CHMe{\cdot}OH$ (XVI)

$(EtO_2C)_2CH{\cdot}CO{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO{\cdot}CH(CO_2Et)_2$ (XVII)

Condensation of muconyl chloride with ethyl malonate readily gave (XVII), which had light-absorption properties indicating that it existed in the dienolic form. Attempts to convert this tetra-ester into (II) by hydrolysis and decarboxylation were unsuccessful, only muconic acid being isolated. This result is in keeping with the recently reported behaviour of related β-ketomalonates (Eisner, Elvidge, and Linstead, *J.*, 1951, 1501).

Experimental

M.p.s are uncorrected. Light-absorption data were determined in ethanol.

Commercial lithium aluminium hydride (*ca.* 80% pure) was used without purification.

For the oxidation experiments manganese dioxide was selected from various commercial sources (cf. Weedon and Woods, *J.*, 1951, 2687). Acetone was treated with potassium permanganate and dried (K_2CO_3). Unless stated otherwise, oxidations of (IV) were performed by shaking a solution of the crude distilled product in acetone (100 vols.) with manganese dioxide (20 parts by weight) at room temperature.

All chromatograms were carried out on alumina (Grade II—III; cf. Brockmann and Schodder, *Ber.*, 1941, **74**, 73) which had been pretreated as described in Part XXXV (*J.*, 1949, 3120).

Syntheses from Dihydromuconic and Muconic Acids.—Δ^{β}-Dihydromuconic acid. A mixture of 1 : 4-dibromobut-2-ene (360 g.), acetonitrile (720 c.c.; technical), and cuprous cyanide (360 g.) was heated under reflux (steam-bath) until reaction commenced, then cooled (ice-bath; until the vigorous reaction had subsided), and finally heated under reflux for 1 hour, again cooled, and, when cuprous bromide began to separate, poured into ether. The suspension was filtered and the filtrate evaporated, giving a mixture (*ca.* 130 g.) of 1 : 2 : 3 : 4-tetrabromobutane and 1 : 4-dicyanobut-2-ene. This was added to concentrated hydrochloric acid (750 c.c.), and the mixture was boiled for 3 hours whereupon the tetrabromide steam-distilled and collected in the condenser.

The clear red acid solution was cooled in ice; Δ^{β}-dihydromuconic acid (76 g.) which separated had m. p. 193—194°, raised to 195° by one recrystallisation from water (Bode, *Annalen*, 1889, **256**, 26, gives m. p. 195°).

In one experiment (from 80 g. of dibromobutene) the crude dinitrile was crystallised from benzene–light petroleum (b. p. 40—60°), giving 1 : 4-dicyanobut-2-ene (20 g., 50%) as needles, m. p. 76—77° (Hager, U.S.P. 2,462,388, gives m. p. 75—77°).

Oct-4-ene-2 : 7-dione. Dihydromuconic acid (40 g.) and thionyl chloride (240 c.c.), heated under reflux for 4 hours, gave dihydromuconyl chloride (47 g.), b. p. 83—84°/10^{-3} mm., n_D^{19} 1·4920.

Powdered cadmium chloride (20 g.; dried by heating it just below the m. p. for 20 minutes) was added in several portions to a stirred solution of methylmagnesium bromide (from 4·5 g. of magnesium) in ether (150 c.c.), and the suspension was heated under reflux for ½ hour. (A small portion gave no colour with the Gilman reagent, indicating complete conversion of the Grignard complex into dimethylcadmium; cf. Cason, *Chem. Reviews*, 1947, **40**, 15.) The ether was then distilled off and benzene (140 c.c.) was added. The above acid chloride (4·7 g.) in benzene (20 c.c.) was added dropwise, and the mixture was heated under reflux for 1 hour and then cooled (ice-bath). Dilute sulphuric acid was added, and the benzene layer was separated, washed with sodium hydrogen carbonate solution, dried, and evaporated under reduced pressure. A portion (1·6 g.) of the residue (2·0 g.) was distilled and the fraction (0·6 g.), b. p. 75—85°/10^{-3} mm., was collected; on cooling this solidified. Two crystallisations from light petroleum (b. p. 60—80°) gave oct-4-ene-2 : 7-dione as plates, m. p. 35—36° (Found: C, 68·4; H, 9·0. Calc. for $C_8H_{12}O_2$: C, 68·55; H, 8·65%) (Karrer and Eugster, *Helv. Chim. Acta*, 1949, **32**, 1934, give m. p. 31°). The *bis*-2 : 4-*dinitrophenylhydrazone* crystallised from nitromethane in orange plates, m. p. 208—209° (Found: C, 48·1; H, 4·15; N, 22·55. $C_{20}H_{20}O_8N_8$ requires C, 48·0; H, 4·05; N, 22·4%).

In some experiments under conditions nearly identical with those described above, the diketone was obtained admixed with polymer and varying amounts of 2 : 7-*dimethyloct-4-ene-2 : 7-diol*. The latter crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 86° (Found: C, 69·4; H, 11·4. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7%). Hydrogenation of this in ethyl acetate in the presence of Adams's catalyst gave 2 : 7-dimethyloctane-2 : 7-diol which crystallised from ether–light petroleum (b. p. 40—60°) in needles, m. p. 92—93°, and from water in plates, m. p. 58—59° (Zal'kind and Aizikovich, *J. Gen. Chem., Russia*, 1937, **7**, 227, give m. p. 88—89°, from light petroleum, and 57—59°, from water). The formation of a tertiary alcohol on reaction of an acid chloride with dimethylcadmium has also been reported by Pinson and Friess (*J. Amer. Chem. Soc.*, 1950, **72**, 5333).

Octa-3 : 5-diene-2 : 7-dione. A mixture of muconic acid (7·1 g.) (Guha and Sankaran, *Org. Synth.*, 1946, **26**, 57) and thionyl chloride (45 c.c.) was heated under reflux for 25 hours. The resulting solution was evaporated under reduced pressure, giving crude muconyl chloride (cf. Bailey and Ross, *J. Amer. Chem. Soc.*, 1949, **71**, 2570). A solution of this in benzene (30 c.c.) was added to dimethylcadmium (from 4·9 g. of magnesium and 19·6 g. of cadmium chloride) in benzene (175 c.c.). The mixture was heated to *ca.* 60° for 1 hour and then cooled. Sulphuric acid (2N) was added and the crude product (4·6 g.) was isolated and distilled. The fraction, b. p. <80°/10^{-2} mm., partly solidified. Recrystallisation from light petroleum (b. p. 60—80°) gave octa-3 : 5-diene-2 : 7-dione (100 mg.) as needles, m. p. 126—127°. Light absorption: max., 2720 and 2790 Å; ε, 31,000 and 32,000, respectively (Karrer, Eugster, and Perl, *Helv. Chim. Acta*, 1949, **32**, 1013, give m. p. 126—126·5°; max., 2760 Å; ε, 33,000).

Ethyl 2 : 7-diketo-octa-3 : 5-diene-1 : 1 : 8 : 8-tetracarboxylate. Muconyl chloride (3·75 g.) in ether (50 c.c.) was added during 20 minutes to a stirred solution of sodiomalonate (from 3 g. of sodium and 30 c.c. of ethyl malonate) in ether (300 c.c.). The mixture was heated under reflux for 1·5 hours and then cooled. Sulphuric acid (2N) was added and the ethereal layer was separated, washed with sodium hydrogen carbonate solution, dried, and evaporated. The residue was triturated with light petroleum (b. p. 40—60°). The solid (6·1 g.), m. p. 124—128°, was recrystallised from alcohol, giving the *tetraester* as long yellow needles (5·1 g.), m. p. 132° (Found: C, 56·35; H, 6·25. $C_{20}H_{26}O_{10}$ requires C, 56·3; H, 6·15%). Light absorption: max., 3550 Å; ε, 51,000: inflexion, 3620 Å; ε, 45,000.

Syntheses from Octa-3 : 5-diyne-2 : 7-diol.—Octa-3 : 5-diene-2 : 7-diol. Octa-3 : 5-diyne-2 : 7-diol (10·0 g.; mixture of stereoisomers) (Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1578) in ether (100 c.c.) was added during 45 minutes to a stirred solution of lithium aluminium hydride (4·5 g.) in ether (600 c.c.). The mixture was heated under reflux for 15 hours and the excess of hydride then destroyed by the addition of ethyl acetate. The mixture was cooled

(0°), a cold solution of ammonium chloride was added, and the ethereal layer was separated, washed with water, and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue gave the crude glycol as a viscous oil (7·6 g.), b. p. 90—100° (bath temp.)/10^{-4} mm., n_D^{23} 1·5085.

Similar reductions of octa-3 : 5-diyne-2 : 7-diol were also performed but with larger proportions of lithium aluminium hydride ; the results are given in the following table.

Mols. of hydride *	1·3	1·7	2·4	2·6	3·5
Product, b. p. 90—100° (bath)/10^{-4} mm. ; yield, %	74	72	58	50	41
Product, b. p. 90—100° (bath)/10^{-4} mm. ; octa-3 : 5-diene-2 : 7-diol content, % †	64	—	—	74	83

* Allowance has been made for impurities in the commercial hydride used.

† Estimated on the intensity of the 2270-Å absorption maximum, the pure glycol, m. p. 45°, having $E_{1\,cm.}^{1\%} = 2300$. The purity, 64%, for the product obtained by using 1·3 mols. of hydride was subsequently confirmed by oxidation, whereby (II) was isolated in 58% yield (*i.e.*, 91% based on the estimated amount of diene glycol).

The *dibenzoate* (*ca.* 20% yield) crystallised from methanol in needles, m. p. 80° (Found : C, 75·6; H, 6·45. $C_{32}H_{22}O_4$ requires C, 75·5; H, 6·35%). Light absorption : max. 2270 Å; ε, 64,000. A mixture of the dibenzoate (1·0 g.) in benzene (5 c.c.) and methanolic potassium hydroxide (10% w/v; 5 c.c.) was heated under reflux for 10 minutes and then cooled. Water was added and the product isolated with ether, giving an oil, b. p. 90—95° (bath-temp.)/10^{-4} mm., which solidified at 0°. Crystallisation from *cyclo*hexane gave *octa*-3 : 5-*diene*-2 : 7-*diol* (164 mg.) as needles, m. p. 45° (Found : C, 67·3; H, 9·95. $C_8H_{14}O_2$ requires C, 67·5; H, 9·95%). Light absorption : see Table 1.

Octa-3 : 5-*diene*-2 : 7-*dione*. (*a*) A solution of the crystalline 2 : 7-diol (150 mg.) in acetone (15 c.c.) was shaken with manganese dioxide (3 g.) at 20° for 24 hours. The mixture was filtered, the solid was washed thoroughly with acetone, and the combined filtrate and washings were evaporated. Crystallisation of the residue, m. p. 120—122°, from alcohol gave the diketone (106 mg.) as needles, m. p. 124° (Found : C, 69·5; H, 7·5. Calc. for $C_8H_{10}O_2$: C, 69·45; H, 7·3%). Light absorption : max., 2800 Å; ε, 32,000 : inflexion, 2730 Å; ε, 29,500.

Oxidation in the above manner of the liquid glycol (64%-pure) (10·0 g.), without regeneration from the dibenzoate, gave an oil from which the diketone (2·6 g.) separated. Re-oxidation of the residual oil gave more (3·0 g.) diketone. The total yield of crystalline diketone, m. p. 124°, was 58% (based on crude glycol). The bis-semicarbazone had m. p. 249° (Karrer, Eugster, and Perl, *loc. cit.*, give m. p. 249°).

In small-scale experiments (*ca.* 1—3 g. of crude glycol) carried out as described above but by using single reaction periods of 12, 24, and 70 hours, the yields of crystalline diketone were 35, 50, and 50%, respectively.

(*b*) A solution of the diacetylenic glycol (6·2 g.) in methanol (40 c.c.) was shaken in the presence of palladium–charcoal (0·5 g.; 4% of Pd), partially poisoned by quinoline (cf. Isler, Huber, Ronco, and Kofler, *Helv. Chim. Acta*, 1947, **30**, 1911), until 1·6 mols. of hydrogen had been absorbed (cf. Inhoffen, Pommer, Winkelmann, and Aldag, *Chem. Ber.*, 1951, **84**, 87). The reaction was interrupted, the catalyst and solvent were removed, and the residue was distilled, giving the crude diene glycol (4·8 g.), b. p. 90—100° (bath-temp.)/10^{-4} mm., n_D^{19} 1·4927. Light absorption : max., 2300 Å, $E_{1\,cm.}^{1\%}$ 850.

Oxidation (24 hours) of the crude glycol (4·2 g.) gave a dark brown oil (3·8 g.) which was purified by chromatographic adsorption on alumina from benzene solution. The oil (1·3 g.) thus obtained had a light absorption max. at 2750 Å ($E_{1\,cm.}^{1\%}$ 700). On cooling, it deposited octa-3 : 5-diene-2 : 7-dione (220 mg.), m. p. 124—126°.

Oct-4-*ene*-2 : 7-*dione*.—Octa-3 : 5-diene-2 : 7-dione (4·0 g.), reduced with zinc dust and acetic acid in pyridine by Karrer and Eugster's method (*Helv. Chim. Acta*, 1949, **32**, 1934), gave oct-4-ene-2 : 7-dione (3·2 g.), m. p. 31—32°. The bis-2 : 4-dinitrophenylhydrazone had m. p. 208—209°, undepressed on admixture with the specimen described above.

Syntheses from Oct-6-*en*-3-*yne*-2 : 5-*diol*.—*Oct*-6-*en*-3-*yne*-2 : 5-*diol*. Ether was displaced from a solution of ethylmagnesium bromide (from 24 g. of magnesium) in ether (400 c.c.) by distillation while benzene (600 c.c.) was added. The solution was cooled in an ice-bath and hex-4-en-1-yn-3-ol (40 g.) in benzene (120 c.c.) was added during ½ hour. The mixture was stirred at 20° for 3 hours and then again cooled in an ice-bath. Acetaldehyde (44 g.) in benzene (100 c.c.) was added during ½ hour. After the mixture had been stirred at 20° for 1 hour, the complex was decomposed by addition of a saturated aqueous solution of ammonium chloride. Isolation of the product gave (i) recovered alcohol (15·0 g.) and (ii) the *glycol* (49·8 g.), b. p. 124°/0·02 mm.

n_D^{20} 1·4960 (Found: C, 68·1; H, 8·6. $C_8H_{12}O_2$ requires C, 68·5; H, 8·65%). The glycol exhibited no light absorption of appreciable intensity in the 2000—4000-Å range.

When the suspension of the Grignard complex of hex-4-en-1-yn-3-ol in benzene was warmed, and the mixture heated to 70° for 1 hour after the addition of acetaldehyde, considerable polymerisation occurred and the yield of glycol was negligible.

Oct-3-en-5-yne-2 : 7-diol. (*a*) A solution of oct-6-en-3-yne-2 : 5-diol (3·9 g.) in sulphuric acid (135 c.c.; 15% wt./vol.) was kept at 20° for 1·5 hours. The solution was then neutralised by the addition of solid sodium hydrogen carbonate, and saturated with ammonium sulphate. The product was extracted with ether. Distillation gave the *glycol* (3·7 g.), b. p. 85—90° (bath-temp.)/10^{-4} mm., n_D^{21} 1·5130 (Found: C, 68·35; H, 8·7. $C_8H_{12}O_2$ requires C, 68·5; H, 8·65%). Light absorption: max., 2280 Å; ε, 12,500: inflexion. 2340 Å: ε, 9500.

(*b*) A solution of hex-3-en-5-yn-2-ol (44·0 g.) in benzene (100 c.c.) was added slowly to an ice-cooled solution of ethylmagnesium bromide (from 26·5 g. of magnesium) in benzene (900 c.c.). The solution was stirred for 3 hours at 20° and again cooled to 0°. Acetaldehyde (48·5 g.) in benzene (100 c.c.) was added during ½ hour and the mixture stirred for 2 hours at 20°. Decomposition of the complex and isolation of the product gave (i) recovered alcohol (10·0 g.) and (ii) the glycol (34—39 g.), b. p. 107—110°/10^{-3} mm., b. p. 90° (bath-temp.)/10^{-4} mm., n_D^{19} 1·5141. Light absorption: max., 2270 Å; ε, 13,500: inflexion, 2350 Å; ε, 11,500.

Octa-3 : 5-diene-2 : 7-diol and octa-3 : 5-diene-2 : 7-dione. (*a*) A solution of oct-3-en-5-yne-2 : 7-diol (12·0 g.) in methanol (150 c.c.) was shaken in hydrogen in the presence of palladium–charcoal (1·5 g.; 4% of Pd), partly poisoned by quinoline (cf. Isler, Huber, Ronco, and Kofler, *loc. cit.*) until one mol. had been absorbed (2090 c.c. at 20°/760 mm.). After removal of catalyst and solvent the residue was distilled, giving the crude diene glycol (9·5 g.), b. p. 90—100° (bath-temp.)/10^{-4} mm., n_D^{26} 1·4997. Light absorption: max. 2270 Å; $E_{1\,cm}^{1\%}$ 700. (In other experiments performed similarly the product had $E_{1\,cm.}^{1\%}$ up to 1300.)

Oxidation (72 hours) of the crude glycol (3·4 g.) and chromatographic purification of the product (3·4 g.) gave octa-3 : 5-diene-2 : 7-dione (180 mg., 5% overall yield), m. p. 124° undepressed on admixture with the above specimen from the diacetylenic glycol (III).

(*b*) The glycol (1·2 g.) in ethyl acetate (10 c.c.) was partly hydrogenated, giving the impure diene glycol (1·2 g.), b. p. 90—100° (bath-temp.)/10^{-4} mm., n_D^{20} 1·4935. Light absorption: max., 2300 Å; $E_{1\,cm.}^{1\%}$ 1200. Oxidation (24 hours) gave the diketone (190 mg., 14% overall yield), m. p. and mixed m. p. 124—125°.

(*c*) A solution of oct-3-en-5-yne-2 : 7-diol (5·0 g.) in ether (50 c.c.) was added during ½ hour to lithium aluminium hydride (1·2 g.) in ether (200 c.c.). The mixture was heated under reflux for 15 hours and then cooled. Isolation of the product gave the crude diene glycol (4·2 g.), b. p. 90—100° (bath-temp.)/10^{-4} mm., n_D^{25} 1·5065. Light absorption: max., 2270 Å; $E_{1\,cm.}^{1\%}$ 1350: inflexion, 2330 Å; $E_{1\,cm.}^{1\%}$ 1200. Oxidation (48 hours) gave the diketone (315 mg., 8% overall yield), m. p. and mixed m. p. 125°.

7-2′-Tetrahydropyranyloxyoct-5-en-3-yn-2-ol.—A solution of phenyl-lithium (from 1·6 g. of lithium) was added dropwise to a solution of 2-2′-tetrahydropyranyloxyhex-3-en-5-yne (20 g.) [prepared from hex-3-en-5-yn-2-ol and dihydropyran (Bharucha and Weedon, *loc. cit.*)] in ether (150 c.c.), and the mixture stirred at 0° for 16 hours. Acetaldehyde (9 g.; freshly distilled) in ether (75 c.c.) was added slowly and the temperature of the mixture allowed to rise to 20° during 8 hours. The mixture was then heated under reflux for 10 minutes and cooled. Decomposition of the complex with ammonium chloride and isolation of the product with ether gave the *alcohol* (19·5 g.), b. p. 80—90° (bath temp.)/10^{-4} mm., n_D^{24} 1·4941 (Found: C, 70·3; H, 9·05. $C_{13}H_{20}O_3$ requires C, 69·65; H, 8·9%). Light absorption: max., 2270 Å; ε, 17,000.

7-2′-Tetrahydropyranyloxyocta-3 : 5-dien-2-ol. Lithium aluminium hydride (1·3 g.) in ether (75 c.c.) was added during 30 minutes to a solution of the preceding alcohol (10·0 g.) in ether (100 c.c.), and the mixture was heated under reflux for 3 hours and then cooled. Decomposition of the complex and isolation of the product gave the *diene* (7·2 g.), b. p. 80—85° (bath-temp.)/10^{-4} mm., n_D^{21} 1·4947 (Found: C, 68·75; H, 10·15. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·75%). Light absorption: max., 2270 Å; ε, 24,000.

Octa-3 : 5-diene-2 : 7-dione. A solution of the preceding diene (4·8 g.) in methanolic sulphuric acid (2N; 200 c.c.) was kept at 20° for 3 hours. The acid was neutralised by the addition of solid sodium carbonate, and the mixture was filtered. Evaporation of the filtrate and isolation of the product from the residue by ether gave an oil (1·9 g.), oxidation (24 hours) of which gave a product which on cooling (alcohol–carbon dioxide) deposited a solid (124 mg.), m. p. 117—120°. One recrystallisation from alcohol gave octa-3 : 5-diene-2 : 7-dione, m. p. and mixed m. p. 124°.

Octa-3 : 6-diene-2 : 5-diol. A solution of oct-6-en-3-yne-2 : 5-diol (8·5 g.) in ethyl acetate

(50 c.c.) was shaken in an atmosphere of hydrogen in the presence of palladium–calcium carbonate (1·0 g.; 0·27% of Pd) until one mol. of hydrogen had been absorbed (1480 c.c. at 17°/756 mm.). The catalyst and solvent were removed and the residue was distilled, giving the *glycol* (7·6 g.), m. p. 85°/0·006 mm., n_D^{23} 1·4859 (Found: C, 67·7; H, 9·75. $C_8H_{14}O_2$ requires C, 67·55; H, 9·95%).

When the hydrogenation was carried out in methanolic solution with 10% palladium–calcium carbonate, there was obtained a 60% yield of a liquid, b. p. 30—170°/10^{-3} mm., n_D^{20} 1·4480—1·5093, from which no pure compound could be isolated.

Rearrangement of octa-3 : 5-diene-2 : 5-diol. A solution of the unconjugated glycol (6·0 g.) in sulphuric acid (300 c.c.; 0·2% wt./vol.), containing a trace of quinol, was kept at 20° for 1·5 hours. The solution was neutralised with sodium hydrogen carbonate and saturated with ammonium sulphate, the product was extracted with ether, and the ethereal solution was washed with water, dried, and evaporated. This gave a mixture of the conjugated glycols, octa-3 : 5-diene-2 : 7-diol and octa-4 : 6-diene-2 : 3-diol, as an oil (5·5 g.), n_D^{20} 1·5100. A small portion was distilled for analysis and had b. p. 80° (bath-temp.)/10^{-4} mm., n_D^{20} 1·5102 (Found: C, 67·3; H, 9·85. Calc. for $C_8H_{14}O_2$: C, 67·55; H, 9·95%). Light absorption: max., 2290 Å; ε, 25,500.

When the rearrangement was carried out with 1% acid for 60 hours, an appreciable amount of low-boiling material was obtained and the yield of glycols was reduced to 40%.

Octa-3 : 5-diene-2 : 7-dione. Oxidation (24 hours) of the preceding mixture (1·0 g.) and chromatographic purification of the crude product gave octa-3 : 5-diene-2 : 7-dione (70 mg.), m. p. 125°.

Octane-2 : 7- and -2 : 3-diols. Hydrogenation (Adams's catalyst) of the mixture (2·6 g.) of glycols in methanol (30 c.c.) (absorption, 880 c.c. at 19°/765 mm., equiv. to 2·0 double bonds), removal of catalyst and solvent, and distillation gave mixed saturated glycols (2·2 g.), b. p. 95—96°/0·01 mm., n_D^{20} 1·4515 (Found: C, 65·5; H, 12·2. Calc. for $C_8H_{18}O_2$: C, 65·7; H, 12·4%).

A portion of the mixture was treated at 20° with an excess of sodium periodate solution. At intervals aliquots of the resulting solution were added to an excess of potassium iodide solution, and the iodine liberated was titrated with sodium thiosulphate solution. The titre became constant after 36 hours and indicated that the original mixture contained 58% of the α-glycol.

Octane-2 : 7-dione. (*a*) A solution of the saturated glycols (1·5 g.) in acetone (3 c.c.) was treated at 0° with a solution of chromium trioxide (0·8 g.) and concentrated sulphuric acid (0·8 c.c.) in water (2 c.c.). The product was extracted with ether, and the extract was washed thoroughly with sodium hydrogen carbonate solution and water, dried ($MgSO_4$), and evaporated. Of the residual crude octa-2 : 7-dione, one half was treated with methanolic semicarbazide acetate and the other with methanolic 2 : 4-dinitrophenylhydrazine sulphate. The bis-semicarbazone (255 mg.) crystallised from dimethylformamide and had m. p. 221·5° undepressed on admixture with a specimen from (*b*). The bis-2 : 4-dinitrophenylhydrazone (520 mg.) crystallised from nitromethane and had m. p. 208°, undepressed on admixture with a sample from (*b*).

(*b*) Hydrogenation (Adams's catalyst, 25 mg.) of octa-3 : 5-diyne-2 : 7-diol (0·8 g.) in methanol (15 c.c.) (absorption, 630 c.c. at 18°/761 mm., equiv. to 4·5 double bonds), removal of catalyst and solvent, and oxidation of the residue as in (*a*), gave a crude diketone, whose bis-semicarbazone, crystallised from dimethylformamide, had m. p. 222° (Meerwein, *Annalen*, 1914, **405**, 159, gives m. p. 223°). The *bis-2 : 4-dinitrophenylhydrazone*, crystallised from methanol–nitromethane (1 : 1), had m. p. 209° (Found: N, 22·55. $C_{20}H_{22}O_8N_8$ requires N, 22·3%).

Periodate fission of octa-4 : 6-diene-2 : 3-diol. (*a*) A solution of the mixed conjugated glycols, octa-3 : 5-diene-2 : 7-diol and octa-4 : 6-diene-2 : 3-diol (0·5 g.), and sodium periodate (2·0 g.) in water was steam-distilled. The distillate was collected in a solution of 2 : 4-dinitrophenylhydrazine sulphate in water, and distillation was continued until no more solid separated in the receiver. The solid was collected and dried (1·21 g., 70%). A benzene solution was poured on a column of alumina (200 g.) and the chromatogram developed with the same solvent. The main diffuse brown band yielded a red crystalline solid (0·91 g.), which was dissolved in boiling ethyl acetate and the solution cooled to *ca.* 30°, giving a dark red powder (350 mg.), m. p. 179—181°. This was filtered off and crystallised from ethyl acetate, giving sorbaldehyde 2 : 4-dinitrophenylhydrazone, m. p. 192° undepressed on admixture with an authentic specimen, m. p. 193°. When the original ethyl acetate mother-liquors cooled, an orange powder (300 mg.), m. p. 153—157°, separated. This was crystallised first from light petroleum (b. p. 60—80°) and then from alcohol, giving acetaldehyde 2 : 4-dinitrophenylhydrazone as plates, m. p. 164° undepressed on admixture with an authentic specimen.

(*b*) A solution of the mixed conjugated glycols (3·7 g.) and sodium periodate (6·4 g.) in water

(100 c.c.) was steam-distilled. The aqueous distillate (175 c.c.) was neutralised with sodium hydrogen carbonate, saturated with ammonium sulphate, and extracted with ether. The extract was dried ($MgSO_4$) and evaporated, and the residual oil treated with an excess of methanolic semicarbazide acetate solution. The crude derivative was crystallised once from aqueous methanol, giving sorbaldehyde semicarbazone (2·0 g., 50% based on mixture of glycols) as plates, m. p. 205° undepressed on admixture with an authentic specimen, m. p. 206°.

(*c*) A solution of octa-3 : 6-diene-2 : 5-diol (7·6 g.) in sulphuric acid (400 c.c.; 0·2% wt./vol.) was kept at 20° for 90 minutes. Sodium periodate (10 g.) was added and the mixture steam-distilled. Isolation of the product as described in (*b*) and conversion of the crude sorbaldehyde (3·2 g.), n_D^{20} 1·530, into the semicarbazone gave plates (3·0 g., 37% based on the diol), m. p. 204° undepressed on admixture with an authentic specimen.

Rearrangement of the diol with 0·5% acid and subsequent treatment as detailed above gave sorbaldehyde semicarbazone in 29% yield.

Rearrangement of octa-3 : 5-diene-2 : 7-diol. A solution of octa-3 : 5-diene-2 : 7-diol (0·94 g., 64% pure), in sulphuric acid (50 c.c.; 0·2% wt./vol.), was kept at 20° for 90 minutes. Sodium periodate (2·5 g.) was added and the mixture was steam-distilled. The distillate was collected in aqueous 2 : 4-dinitrophenylhydrazine sulphate, and the resulting crude derivative was purified by chromatography on alumina, giving a red powder (20·4 g.), m. p. 178°. Crystallisation from ethyl acetate yielded sorbaldehyde 2 : 4-dinitrophenylhydrazone (10 mg.), m. p. 193°, undepressed on admixture with an authentic specimen.

Syntheses from 2-Methyloct-6-en-3-yne-2 : 5-diol.—2-Methylocta-3 : 6-diene-2 : 5-diol. 2-Methyloct-6-en-3-yne-2 : 5-diol was prepared in 85% yield from hex-4-en-1-yn-3-ol and acetone as described above for oct-6-en-3-yne-2 : 5-diol (cf. Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39). A solution of this glycol (15·5 g.) in ethyl acetate (75 c.c.) was shaken in hydrogen in the presence of a palladium–calcium carbonate catalyst (1·5 g.; 0·27% of Pd) until 1 mol. of hydrogen had been absorbed (2417 c.c. at 18°/760 mm.). The catalyst and solvent were removed and the residue distilled, giving the *glycol* (13·9 g.), b. p. 85—87°/0·02 mm., n_D^{25} 1·4742—1·4763 (Found : C, 69·35; H, 10·45. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). Light absorption : max., 2280 and 2360 Å; $E_{1\,cm.}^{1\%}$ 90 and 90.

Rearrangement of 2-methylocta-3 : 6-diene-2 : 5-diol. A solution of the glycol (10·2 g.) in sulphuric acid (500 c.c.; 0·2% wt./vol.) was kept at 20° for 90 minutes. Isolation of the product gave a mixture of the conjugated glycols (5·2 g.), b. p. 89°/0·002 mm., n_D^{26} 1·4929 (Found : C, 69·2; H, 10·5. Calc. for $C_9H_{16}O_2$: C, 69·2; H, 10·3%). Light absorption : max., 2280 Å; ε, 20,000 : inflexion, 2340 Å; ε, 17,500.

Periodate fission of 2-methylocta-4 : 6-diene-2 : 3-diol. (*a*) A solution of the preceding conjugated glycols (3·0 g.) in ether (10 c.c.) was shaken with a solution of sodium periodate (4·5 g.) in water (150 c.c.) at 20° for 15 hours. The aqueous layer was saturated with ammonium sulphate and the product isolated with ether and treated with an excess of semicarbazide acetate in methanol. This gave sorbaldehyde semicarbazone which crystallised from methanol in plates (1·5 g., 51% based on mixture of glycols), m. p. 206° undepressed on admixture with an authentic specimen.

(*b*) The conjugated glycols (0·74 g.) were added to a solution of sodium periodate (1·1 g.) in water (30 c.c.), and the mixture was steam-distilled. The distillate was collected in a flask containing a solution of dimedone (1·5 g.) in alcohol (60 c.c.) and water (15 c.c.). The resulting yellow emulsion was kept at 20° for ½ hour and then at 0° for 2 hours. The solid was filtered off and the filtrate was steam-distilled. The distillate was collected in aqueous 2 : 4-dinitrophenylhydrazine sulphate (from 1·5 g. of 2 : 4-dinitrophenylhydrazine); acetone 2 : 4-dinitrophenylhydrazone (590 mg.; 52% based on mixture of glycols), m. p. 128° undepressed on admixture with an authentic specimen, m. p. 129°, was obtained.

(*c*) 2-Methylocta-6-en-3-yne-2 : 5-diol (7·75 g.) was partially hydrogenated; the resulting crude ethylenic glycol was dissolved in sulphuric acid (350 c.c.; 0·2% wt./vol.), and the solution kept at 20° for 1·5 hours. Sodium periodate (8·0 g.) was added and the mixture steam-distilled. Isolation of the product with ether gave crude sorbaldehyde (1·45 g.; 30%), b. p. 47—49°/15 mm., n_D^{22} 1·536. Light absorption : max., 2800 Å; $E_{1\,cm.}^{1\%}$ 1940, indicating a purity of 80—85%. The 2 : 4-dinitrophenylhydrazone had m. p. 193°, undepressed on admixture with an authentic specimen.

Syntheses from Dec-2-en-5-yne-4 : 7-diol.—Deca-2 : 5-diene-4 : 7-diol. Dec-2-en-5-yne-4 : 7-diol was prepared in 83% yield from hex-4-en-1-yn-3-ol and *n*-butaldehyde in the manner described above for oct-6-en-3-yne-2 : 5-diol (cf. Cymerman, Heilbron, Johnson, and Jones, *J.*, 1944, 141). A solution (7·1 g.) in ethyl acetate (75 c.c.) was shaken in hydrogen in the presence

of a palladium–calcium carbonate catalyst (1·0 g.; 0·27% Pd) until 1 mol. of hydrogen had been absorbed (1050 c.c. at 17°/750 mm.). Isolation of the product gave the *decadienediol* (4·5 g.), b. p. 117°/0·002 mm., n_D^{25} 1·4800—1·4830 (Found: C, 70·7; H, 10·8. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). Light absorption: max., 2290 and 2630 Å; $E_{1\,cm.}^{1\%}$ 90 and 55, respectively. The *bis*-3 : 5-*dinitrobenzoate* crystallised from methanol–benzene (1 : 1) and had m. p. 156° (Found: N, 10·05. $C_{24}H_{22}O_{12}N_4$ requires N, 10·05%).

Rearrangement of deca-2 : 5-*diene*-4 : 7-*diol.* A mixture of the decadienediol (4·0 g.), sulphuric acid (200 c.c.; 0·2% wt./vol.), and a trace of quinol was shaken at 20° for 2 hours. The mixture was neutralised by the addition of sodium hydrogen carbonate, and the aqueous layer was saturated with ammonium sulphate. Isolation of the product with ether and distillation gave a mixture of the isomeric conjugated glycols (3·1 g.), b. p. 98°/0·003 mm., n_D^{19} 1·4970 (Found: C, 70·8; H, 10·8. Calc. for $C_{10}H_{18}O_2$: C, 70·55; H, 10·65%). Light absorption: max. 2290 Å; ε, 19,500.

Periodate fission of deca-6 : 8-*diene*-4 : 5-*diol.* Dec-2-en-5-yne-4 : 7-diol (18·9 g.) was partially hydrogenated and the crude product was rearranged by shaking it with sulphuric acid (800 c.c.; 0·2% wt./vol.) for 2 hours at 20°. Sodium periodate (26 g.) was added, the mixture steam-distilled, and the distillate was extracted with ether. The extract was dried and evaporated, finally at 35°/15 mm. for 15 minutes. The residue was treated with an excess of methanolic semicarbazide acetate, giving sorbaldehyde semicarbazone (plates from aqueous methanol) (14·1 g.; 82% based on the acetylenic glycol), m. p. 205° undepressed on admixture with an authentic specimen, m. p. 206°.

Synthesis from Oct-4-*yne*-2 : 7-*diol.*—*Oct*-4-*yne*-2 : 7-*diol.* (*a*) Acetylene was passed into a solution of ethylmagnesium bromide (from 36 g. of magnesium) in benzene (1 l.) for 3 hours; the mixture became warm and a grey solid separated. The suspension was cooled to 0°, propylene oxide (171 g.) was added dropwise, and the mixture was stirred for 2 hours at 20° and then for 15 minutes under reflux. After the mixture had cooled, the complex was decomposed by addition of a saturated aqueous ammonium chloride solution, and the product was isolated. Distillation gave the *octynediol* (46·2 g.), b. p. 102—106°/0·5 mm., n_D^{20} 1·4755 (Found: C, 66·9; H, 9·9. $C_8H_{14}O_2$ requires C, 67·5; H, 9·9%).

(*b*) Pent-4-yn-2-ol (8·4 g.) (Haynes and Jones, *J.*, 1949, 945) in benzene (50 c.c.) was added dropwise to a solution of ethylmagnesium bromide (from 4·85 g. of magnesium) in benzene (100 c.c.). The mixture was stirred for 1 hour at 20° and then for 2 hours under reflux, and cooled. A solution of propylene oxide (5·7 g.) in benzene (25 c.c.) was added during 15 minutes and the mixture was heated under reflux for 1 hour and then cooled. Decomposition of the complex and isolation of the product gave the glycol (4·6 g.), b. p. 95°/0·05 mm., n_D^{19} 1·4759.

cis-*Oct*-4-*ene*-2 : 7-*diol.* A solution of the octynediol (14·0 g.) in ethyl acetate (50 c.c.) was shaken in hydrogen in the presence of a palladium–calcium carbonate catalyst (1·0 g.; 0·3% Pd) until one mol. of hydrogen had been absorbed (2360 c.c. at 17°/757 mm.). The catalyst and solvent were removed and the residue distilled giving the cis-*octenediol* (12·6 g.), b. p. 74°/0·05 mm., n_D^{18} 1·4662 (Found: C, 66·9; H, 11·5. $C_8H_{16}O_2$ requires C, 66·6; H, 11·2%). [For the *trans*-isomer, Karrer and Eugster, *loc. cit.*, give b. p. 90—95° (bath temp.)/0·05 mm.]

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787. *Polymethin Dyes from 4 : 5-Disubstituted Thiazoles.*

By Edward B. Knott

It is shown that α-aryloxy- and α-*p*-tolylthio-acetophenones may be α-brominated and condensed with thioacetamide, to give 4-aryl-5-aryloxy-2-methylthiazoles and 4-aryl-2-methyl-5-*p*-tolylthiothiazoles respectively.* These bases as well as a number of 4 : 5-diaryl-2-methylthiazoles have been quaternized and converted into cyanines, carbocyanines, and dimethin*mero*-cyanines.

In view of the generally strong photographic desensitizing properties of optical sensitizers derived from 4-phenylthiazole it was interesting to note that the red-sensitive layers of certain German colour-photographic products were sensitized by trinuclear dyes containing the 4 : 5-diphenylthiazole nucleus (B.I.O.S. Final Report No. 1355, Item No. 22; U.S. Office, Bureau of Information, Microfilm P.B. 74,175).

Fig. 1.

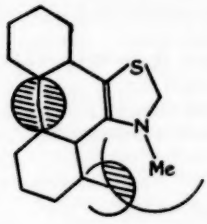


Fig. 2.

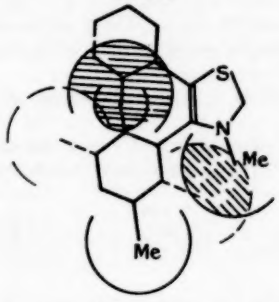
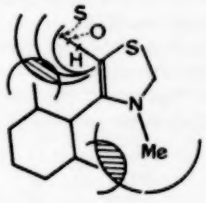


Fig. 3.



A number of cyanines and *mero*cyanines required as intermediates for related complex dyes have now been made from the latter nucleus and the work has been extended to other 4-aryl-5-phenylthiazoles. The requisite intermediates, *i.e.*, 4-aryl-2-methyl-5-phenylthiazoles, were obtained by the normal Hantzsch condensation of substituted α-bromo-α-phenylacetophenones with thioacetamide (cf. Hubacher, *Annalen*, 1890, **259**, 288, for 2-methyl-4 : 5-diphenylthiazole).

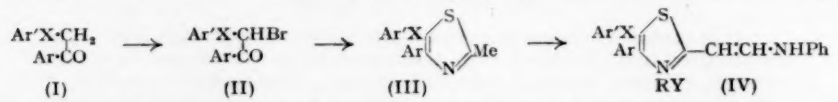
Many of these dyes are good photographic sensitizers but their most interesting property is their much higher solubility in organic solvents compared with closely related dyes from 4-arylthiazoles, benzothiazoles, and naphthothiazoles. This property, in view of the higher molecular weight of the diarylthiazole dyes, is noteworthy and is believed to be due to the fact (see Fig. 1) that the aryl groups are non-planar. The weakening of the cohesive forces in the crystal resulting from a looser packing in order to accommodate the non-planar groups would then be expected to increase the solubility. This is also reflected in the lower melting points of the 4 : 5-disubstituted bases and dyes. To test this theory 2-methyl-5-phenyl-4-*p*-xylylthiazole was synthesised and converted into dyes. As Fig. 2 shows the loss of planarity of the xylyl group must be very great and this is reflected in the high solubilities and low melting points of the dyes. The broken lines in Fig. 2 indicate the alternative position of the xylyl group.

It was then considered that dyes of similarly high solubility might result by replacing one of the aryl groups by other units capable of preventing coplanarity of the remaining aryl group and the rest of the molecule. To this end aryloxy- and arylthio-groups were introduced into the 5-position (Fig. 3). Although the overcrowding here between the 5-substituent and the 2′-hydrogen atom of the 4-phenyl group is much less than in Fig. 1 it

* Since this paper was written, U.S.P. 2,500,142 by Wiesehahn, describing similar condensations, has been brought to my attention.

is sufficient to prevent the 4-phenyl group from bending upwards in order to relieve the overcrowding between the *N*-alkyl group and the 6′-hydrogen of the 4-phenyl group.

Aryloxyacetophenones (I; X = O) and arylthioacetophenones (I; X = S) (*e.g.*,



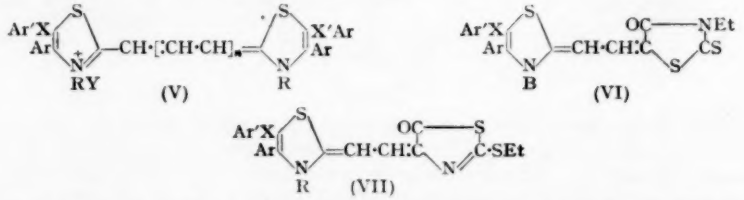
(I) (II) (III) (IV)

Möhlau, *Ber.*, 1882, **15**, 2497; Delisle, *ibid.*, 1889, **22**, 306; Kunckell, *Zentr.*, 1913, II, 153) were brominated smoothly to give well-defined crystalline α-bromo-derivatives (II) which were, for the most part, stable except for the simpler members which decomposed slowly to red solids. They all condensed readily with thioacetamide to give the required 4-aryl-5-aryloxy (or 5-arylthio)-2-methylthiazole (III; X = O or S). This behaviour may be contrasted with that of α-bromo-α-tolylsulphonylacetophenone (II; X = SO_2; Tröger and Müller, *Arch. Pharm.*, 1914, **252**, 51) in which the bromine is not labile to aqueous silver nitrate and which does not give the required thiazole with thioacetamide.

These new thiazoles were quaternized by alkyl toluenesulphonates or sulphates, and the resultant salts condensed with ethyl *iso*formanilide (cf. Knott, *J.*, 1946, 120) to give the required 2-2′-anilinovinyl derivatives (IV). These after acetylation were used to make many of the required dyes. Again the *mero*cyanines were designed as suitable intermediates for complex dyes.

As in the case of the dyes from 4 : 5-diarylthiazole these new dyes were soluble in organic solvents.

In this paper the formation of cyanines (V; $n = 0$), carbocyanines (V; $n = 1$), and dimethin*mero*cyanines (VI and VII) and a few unsymmetrical cyanines is described.



It is of interest that the introduction of substituents into the 4-aryl groups or the replacement of the 4-phenyl by the 4-β-naphthyl group causes little or no effect on the position of the absorption peak (see Experimental section) of any of these dyes. This indicates that the contribution to the dye hybrid by structures in which the positive charge has passed into this group is small. On the other hand the replacement of the 5-phenyl group by the aryloxy- or *p*-tolylthio-group causes a definite hypsochromic shift of 5—10 mμ in both series. In the carbocyanine series the 5-phenoxy-group causes a greater shift (10 mμ) than the 5-*p*-tolylthio-group (5 mμ). The direction of this shift is not unexpected in that, although increased contributions by structures such as (VIII) in which the positive charge passes

beyond the auxochromes would be expected to function bathochromically, the absence of the phenyl groups and such contributing structures as (IX), etc., directly conjugated with $C_{(4)}$—$C_{(5)}$ bond of the thiazole ring will function hypsochromically. The relatively strong bathochromic effect of the presence of this 5-phenyl group is shown by the fact that the removal of this group to give (X) shifts $\lambda_{max.}$ from 548 to 527 mμ, and from the corresponding 3-ethyl-2-thio-5-thiazolid-4-one dye from 548 to 540 mμ.

Experimental

Analyses are by Drs. Weiler and Strauss, Oxford.

α-Bromo-2 : 5-dimethyl-α-phenylacetophenone.—2 : 5-Dimethyl-α-phenylacetophenone (Wege, *Ber.*, 1891, **24**, 3540; b. p. 153°; 112 g., 0·5 mol.) was dissolved in chloroform (400 c.c.) in a 3-necked 1-l. flask fitted with stirrer, dropping funnel, and condenser, leading to an alkali-trap. A solution of bromine (26 c.c., 0·5 mol.) in chloroform (100 c.c.) was dropped in at room temperature. After completed addition the solvent was removed in an air-stream, and the residual *ketone* which soon solidified was obtained as heavy tablets, m. p. 47°, from light petroleum (b. p. 40—60°) in 79% yield (Found : Br, 26·3. $C_{16}H_{15}OBr$ required Br, 26·4%).

4-p-Methoxyphenyl-2-methyl-5-phenylthiazole.—α-Bromo-*p*-methoxy-α-phenylacetophenone (30·1 g., 0·1 mol.) (Meisenheimer and Jochelson, *Annalen*, 1907, **355**, 292), thioacetamide (7·5 g. 0·1 mol.), and methanol (100 c.c.) were warmed on the steam-bath until reaction occurred (*ca.* 1 minute). The methanol boiled, the heating was stopped, and the flask and contents allowed to cool. The required *hydrobromide* (Found : Br, 21·9. $C_{17}H_{16}ONBrS$ requires Br, 22·1%) was precipitated with ether and formed soft needles, m. p. 214° (27·5 g., 77%), from ethanol.

The *base* released with aqueous sodium carbonate formed a thick oil which slowly crystallized. A sample formed thick glassy prisms, m. p. 45°, from light petroleum (b. p. 40—60°) (Found : N, 5·1; S, 11·2. $C_{17}H_{15}ONS$ requires N, 5·0; S, 11·4%).

4-(3 : 4-Dimethoxyphenyl)-2-methyl-5-phenylthiazole.—α-Bromo-3 : 4-dimethoxy-α-phenylacetophenone (67 g., 0·2 mol.) (Kaufmann and Muller, *Ber.*, 1918, **51**, 129), thioacetamide (15 g., 0·2 mol.), anhydrous sodium carbonate (21·2 g., 0·2 mol.), and ethanol (150 c.c.) were refluxed for 15 minutes. Water (250 c.c.) was added to precipitate the *base* as an oil which rapidly crystallised (47 g., 76%). It formed glassy crystals, m. p. 98°, from methanol (Found : N, 4·6; S, 10·2. $C_{18}H_{17}O_2NS$ requires N, 4·5 : S, 10·3%). In one experiment as above, on a 0·01-molar scale, the oil did not crystallize at once. In boiling light petroleum it crystallized and then formed hard aggregates, m. p. 153°, from alcohol (Found : N, 4·4; S, 9·95%).

2-Methyl-4-phenyl-4-p-xylylthiazole.—α-Bromo-2 : 5-dimethyl-α-phenylacetophenone (111 g.), thioacetamide (33·3 g.), and ethanol (110 c.c.) were brought to the b. p. and allowed to cool. Ether (1 l.) was added, to give 88 g. (66·5%) of the hydrobromide. The *base* (66 g.) formed needles, m. p. 72·5°, from light petroleum (Found : N, 5·2; S, 11·9. $C_{18}H_{17}NS$ requires N, 5·0; S, 11·5%).

α-Aryloxyacetophenones (I; X = O).—Potassium hydroxide (1 mole.) was dissolved in boiling alcohol (750 c.c.). The required phenol (1 mole) was then added and the solution cooled to 30°. The addition of the phenacyl bromide (1 mole) with shaking caused a temperature increase to *ca.* 40—45° and separation of potassium bromide. During 1 hour at room temperature, followed by chilling, the required α-aryloxyacetophenone separated. It was collected, washed with ice-cold alcohol (100 c.c.), then much water to remove potassium bromide. The product was often pure enough for the next step. Otherwise it was recrystallized from ethanol. The *products* are reported in Table 1.

Table 1. *α-Aryloxyacetophenones* (I; X = O).

Ar	Ar′	Yield, %	M. p.	Appearance	Formula	Found, %	Req., %
Ph	*p*-C_6H_4Y [a]	50	76°	Flat needles	$C_{32}H_{28}O_2$	C, 81·75	81·5
						H, 8·7	8·65
p-MeO·C_6H_4	,,	90	102	Waxy plates	$C_{33}H_{30}O_3$	C, 78·1	78·0
						H, 8·65	8·5
Ph	*p*-C_6H_4Ph	65	94	Flakes	$C_{20}H_{16}O_2$	C, 83·5	83·4
						H, 5·25	5·55
p-C_6H_4Cl	*p*-C_6H_4Cl	52	132—133	Glossy needles	$C_{14}H_{10}O_2Cl_2$	Cl, 25·3	25·25
p-C_6H_4Br	*p*-C_6H_4Br	63	133—135	Laths	$C_{14}H_{10}O_2Br_2$	Br, 43·15	43·2
3 : 4 : 1-$(MeO)_2C_6H_3$	*p*-EtO·C_6H_4	70	103	Threads	$C_{18}H_{20}O_5$	C, 68·5	68·3
						H, 5·55	5·35
Ph	α-$C_{10}H_7$	79	59	Laths	$C_{18}H_{14}O_2$	C, 82·25	82·5
						H, 5·35	5·35

[a] Y = ·CMe_2·CH_2·CMe_3.

α-p-Tolylthioacetophenones (I; Ar′X = *p*-C_6H_4Me·S)—These *compounds* (see Table 2) were made in the same manner as (I; X = O) (cf. Delisle, *loc. cit.*). In general they separated rapidly as oils from the warm reaction solution and crystallized slowly. They were recrystallized from ethanol or methanol.

TABLE 2. p-*Tolylthioacetophenones* (I; Ar'X = *p*-C_6H_4Me·S).

Ar	Yield, %	M. p.	Appearance	Formula	Found, %	Required, %
Ph	98·5	40°	Needles	$C_{15}H_{14}OS$	C, 74·3; H, 5·8; S, 13·55	C, 74·45; H, 5·8; S, 13·25
2 : 4 : 1-$C_6H_3Me_2$...	88	56	Flakes	$C_{17}H_{17}OS$	S, 12·2	S, 12·3
β-$C_{10}H_7$	93	63	Flakes	$C_{19}H_{16}OS$	S, 10·95	S, 10·95

α-*Bromo-*α-*aryloxy-* (II; X = O) *and* α-*Bromo-*α-p-*tolylthio-acetophenones*.—The ketone (I; X = O or S) (1 mole) in carbon disulphide or chloroform (1 l.) was treated at 5—60° with bromine (1 mole) in the same solvent (250 c.c.). The bromo-ketone was isolated by the removal of the solvent in an air-stream or by washing with dilute aqueous sodium carbonate, then water, drying, and removing the solvent under reduced pressure. The resultant solids or oils were often unstable and were used directly for thiazole formation. The *products* are listed in Table 3.

TABLE 3.

Ar	Ar'	Reaction temp.	Yield	M. p.	Appearance	Formula	Found, % Br	Req., % Br
α-Bromo-α-aryloxyacetophenones (II; X = O).								
Ph	Ph	5—10°	67·5	72°	Needles [a]	$C_{14}H_{11}O_2Br$	27·3	27·45
Ph	*p*-C_6H_4Y [b]	20	95	—	Oil [d]	$C_{22}H_{27}O_3Br$	18·5	19·85
p-MeO·C_6H_4	Ph	5	87	80—81	Needles [a]	$C_{15}H_{13}O_3Br$	24·8	24·9
,,	*p*-C_6H_4Y	5	93	—	Oil [d]	$C_{23}H_{29}O_3Br$	18·1	18·45
Ph	*p*-C_6H_4Ph	20	81	indef.	Powder	$C_{20}H_{15}O_2Br$	21·9	22·5
Ver [b]	*p*-EtO·C_6H_4	35	85	—	Oil	—	—	—
p-C_6H_4Cl ...	*p*-C_6H_4Cl	60	92·5	158	Plates [f, g]	$C_{14}H_9O_2Cl_2Br$	41·45	42·0
p-C_6H_4Br	*p*-C_6H_4Br	55	64	157	Needles [f, g]	$C_{14}H_9O_2Br_3$	53·7	53·5
α-Bromo-α-p-tolylthioacetophenones (II; X = S).								
Ph	—	10	94	79—81	Needles [f]	$C_{15}H_{13}OBrS$	24·65	24·9
p-Xylyl ...	—	30	73	110	Prisms [c, g]	$C_{17}H_{17}OBrS$	22·7	22·9
β-$C_{10}H_7$ ...	—	5	80	119—121	Flakes [c, g]	$C_{19}H_{15}OBrS$	21·75	21·55 [h]

[a] Y = ·CMe_2·CH_2·CMe_3. [b] 3 : 4 : 1-$(MeO)_2C_6H_3$. [c] From light petroleum (b. p. 60—80°). [d] Crude. [e] From light petroleum (b. p. 60—80°). [f] From ethanol. [g] Stable. [h] Found: S, 8·95. Reqd.: S, 8·65%.

4-*Aryl-*5-*aryloxy-*2-*methylthiazoles* (III; X = O).—The bromo-ketone (II; X = O) (1 mole) was dissolved or suspended in ethanol (500 c.c.), and thioacetamide (1·1 mole) added at 30°. There was usually a temperature rise and the mixture was heated, if necessary, to 70°, then allowed to cool. In some cases the required hydrobromide crystallized. In all cases anhydrous ether (2 l.) was added to precipitate all of the hydrobromide. This was collected, made into a slurry in acetone, collected, and washed with acetone. The *base* (see Table 4) was obtained by adding aqueous sodium carbonate to the salt in ethanol. It was usually obtained as a slowly crystallising oil and was then recrystallized from ethanol.

TABLE 4. 4-*Aryl-*5-*aryloxy-*2-*methylthiazoles* (III; X = O).

Ar	Ar'	Yield, %	M. p.	Apearance	Formula	Found, %	Required, %
Ph	Ph	59	63°	Aggreg. [a]	$C_{16}H_{13}ONS$	C, 71·6; H, 4·9; N, 5·5; S, 12·15	C, 71·9; H, 4·85; N, 5·25; S, 12·0
p-MeO·C_6H_4	Ph	64	90	Needles [a]	$C_{17}H_{15}O_2NS$	N, 5·0; S, 10·6	N, 4·7; S, 10·45
Ph	*p*-C_6H_4Y	87	—	Oil [d]	—	—	—
p-MeO·C_6H_4	,, (hydrobromide)	34	186—188	Plates	$C_{25}H_{31}O_2NS$,HBr	Br, 16·5	Br, 16·3
,,	*p*-C_6H_4Y [b]	30	65—72	Needles	$C_{25}H_{31}O_2NS$	N, 3·3; S, 7·45	N, 3·4; S, 7·85
Ph	*p*-C_6H_4Ph	25	102—105	Plates	$C_{22}H_{17}ONS$	C, 81·5; H, 4·9; N, 4·35	C, 82·0; H, 5·25; N, 4·35
Ver [c]	*p*-EtO·C_6H_4	26	71—72	Needles	$C_{20}H_{22}O_4NS$	C, 64·2; H, 5·95; S, 8·5	C, 64·5; H, 5·9; S, 8·6
p-C_6H_4Cl ...	*p*-C_6H_4Cl	33	100—101	Rhombs	$C_{16}H_{11}ONCl_2S$	S, 9·9; Cl, 21·15	S, 9·55; Cl, 21·15

[a] 3 : 4 : 1-$(MeO)_2C_6H_3$. [b] Y = ·CMe_2·CH_2·CMe_3. [c] From light petroleum (b. p. 60—80°). [d] Crude.

4-Aryl-2-methyl-5-p-tolylthiothiazoles (III, Ar'X = *p*-C_6H_4Me·S).—The *compounds* (see Table 5) were obtained as for the above thiazoles except that the reaction was carried out with 1

TABLE 5. *4-Aryl-2-methyl-5-p-tolylthiothiazoles* (III; Ar'X = *p*-C_6H_4Me·S).

Ar	Yield, %	M. p.	Appearance	Formula	Found, % N	Found, % S	Required, % N	Required, % S
Ph	82·5	41—42° (b. p. 200°/6 mm.)	Prisms	$C_{17}H_{15}NS_3$	6·65	21·85	4·7	21·55
3 : 4 : 1-$(MeO)_2C_6H_3$ ...	58	59—60	Needles	$C_{19}H_{19}NS_3$	4·5	19·6	4·3	19·7
β-$C_{10}H_7$	57	93—94	Needles	$C_{21}H_{17}NS_3$	4·2	18·4	4·05	18·4

hour's refluxing before precipitation of the hydrobromides. The bases were recrystallized from light petroleum (b. p. 60—80°).

2-2'-Anilinovinyl-4 : 5-diphenylthiazole Ethotoluene-p-sulphonate.—2-Methyl-4 : 5-diphenylthiazole (12·5 g., 0·05 mol.) (Hubacher, *loc. cit.*) and ethyl toluene-*p*-sulphonate (10 g., 0·05 mol.) were fused at 170° for 4 hours. Ethyl*iso*formanilide (8 g., 0·53 mol.) was added and the whole fused for a further 15 minutes. The whole rapidly solidified with evolution of ethanol. It was ground under acetone, and the solid *salt* collected, washed with acetone, and obtained as a yellow powder (18·2 g., 66%). It formed yellow needles, m. p. 233°, from ethanol (Found: N, 5·0; S, 11·4. $C_{32}H_{30}O_3N_2S_2$ requires N, 5·05; S, 11·55%).

2-2'-Anilinovinyl-4-p-methoxyphenyl-5-phenylthiazole ethotoluene-p-sulphonate, obtained similarly from 4-*p*-methoxyphenyl-2-methyl-5-phenylthiazole in 84% yield, formed yellow-brown needles, m. p. 250°, from ethanol (Found: N, 5·0; S, 10·9. $C_{33}H_{32}O_4N_2S_2$ requires N, 4·8; S, 10·95%). The *methotoluene-p-sulphonate* formed fine, bright yellow needles, m. p. 246° from ethanol (Found: N, 4·85. $C_{32}H_{30}O_4N_2S_2$ requires N, 4·9%).

2-2'-Anilinovinyl-5-phenyl-4-p-xylylthiazole Ethiodide.—2-Methyl-5-phenyl-4-*p*-xylylthiazole (2·74 g., 0·01 mol.) and ethyl sulphate (1·4 c.c., 0·01 mol.) were fused at 150° for 30 minutes. Ethyl*iso*formanilide (1·7 c.c.) was added and fusion continued for a further 30 minutes. The melt was dissolved in ethanol (15 c.c.) and a solution of potassium iodide (2 g.) in water (2 c.c.) added. The *ethiodide* (3·25 g.) separated slowly. It formed violet crystals, m. p. 226°, from ethanol (Found: I, 23·6. $C_{27}H_{27}N_2IS$ requires I, 23·4%).

The *methiodide* (4·3 g.), obtained similarly from the base (2·74 g.) and methyl toluene-*p*-sulphonate (1·9 g.) (30 minutes at 150°), formed light yellow needles, m. p. 247°, from ethanol (Found: I, 24·75. $C_{26}H_{25}N_2IS$ requires I, 24·25%).

2-2'-Anilinovinyl-4-(3 : 4-dimethoxyphenyl)-5-phenylthiazole Ethotoluene-p-sulphonate.—Obtained similarly in 83% yield, this *salt* formed fine yellow needles, m. p. 161°, from ethanol (Found: N, 4·6; S, 10·5. $C_{34}H_{34}O_5N_2S_2$ requires N, 4·65; S, 10·6%).

2-2'-Anilinopropenyl-4-p-methoxyphenyl-5-phenylthiazole Ethiodide.—4-*p*-Methoxyphenyl-2-methyl-5-phenylthiazole etho-*p*-toluenesulphonate (19·0 g.) and ethyl*iso*thioacetanilide (8·0 g.) were fused at 175° for 1 hour, by which time the evolution of ethanethiol had ceased. Ethanol (75 c.c.) was added to the red melt, the whole was heated to dissolution, and an excess of saturated aqueous potassium iodide added. The required *iodide* crystallized on the slow addition of ether. It (16·0 g., 68%) formed garnet-red crystals, m. p. 233°, from ethanol (Found: I, 22·9. $C_{27}H_{25}ON_2SI$ requires I, 22·95%).

2-2'-Anilinovinyl-4-aryl-5-aryloxy(or arylthio)thiazolium Salts (IV).—The above bases (1 mol.) and alkyl ester (1 mol.) were fused at 150—170° until the maximum water solubility of the product was obtained. Ethyl sulphate and methyl toluene-*p*-sulphonate required 90—120 minutes, and ethyl toluene-*p*-sulphonate 5—6 hours. When fusion was completed, ethyl*iso*formanilide (1·1 mols.), was added and the fusion continued at 150° until evolution of ethanol was complete (10—60 minutes). In some cases the melt had then solidified. If not, it was dissolved in ethanol and a solution of potassium iodide (2 mol.) in water added to give the *iodide* which was then crystallized from ethanol. The *salts* prepared are listed in Table 6; all are yellow; most of them form needles.

Unsymmetrical Cyanines.—[*3-Methyl-2-benzothiazole*][*3-ethyl-4-p-methoxyphenyl-4-phenyl-2-thiazole*]*methincyanine iodide.* 4-*p*-Methoxyphenyl-2-methyl-5-phenylthiazole ethotoluene-*p*-sulphonate (0·9 g.), 2-methylthiobenzothiazole methotoluene-*p*-sulphonate (0·7 g.), ethanol (5 c.c.), and triethylamine (0·3 c.c.) were refluxed for 30 minutes. Saturated aqueous potassium iodide (0·5 c.c.) was added and the dye *iodide* (0·95 g.) obtained as greenish-yellow needles, m. p. 304°, from methanol (Found: S, 10·9; I, 21·2. $C_{27}H_{25}ON_2IS_2$ requires S, 10·95; I, 21·75%). $\lambda_{max.}$ 425 mμ in methanol.

TABLE 6.

Ar	Ar′	RY	Yield, %	M. p.	Formula	Found, %	Required, %
2-2′-Anilinovinyl-4-aryl-5-aryloxythiazolium salts (IV; X = O).							
Ph	Ph	EtI	32	196°	$C_{25}H_{23}ON_2IS$ [d]	C, 56·0; H, 4·2	C, 57·0; H, 4·35
p-MeO·C_6H_4	,, ...	,,	38	196	$C_{26}H_{25}O_2N_2IS$	N, 4·9; I, 22·4	N, 5·05; I, 22·85
,,	,,	MeTs [e]	83	202	$C_{32}H_{30}O_5N_2S_2$	N, 4·7; S, 10·7	N, 4·8; S, 10·9
Ph	*p*-C_6H_4Y [b]	EtI	25	176	$C_{33}H_{39}ON_2IS$	I, 19·7	I, 19·9
p-MeO·C_6H_4	,,	MeTs [e]	42	236	$C_{42}H_{46}O_5N_2S_3$	N, 4·05; S, 8·9	N, 3·9; S, 8·9
Ph	*p*-C_6H_4Ph	MeI	72	266	$C_{29}H_{25}ON_2IS$	I, 21·75	I, 22·0
p-C_6H_4Cl ...	*p*-C_6H_4Cl	EtI	46	247	$C_{25}H_{21}ON_2Cl_2IS$	Hal, 33·5	Hal, 33·3
Ver [a]	*p*-EtO·C_6H_4	EtI	48	185	$C_{29}H_{31}O_4N_2IS$	I, 20·5	I, 20·2
2-2′-Anilinovinyl-4-aryl-5-arylthiothiazolium salts (IV; X = S).							
Ph	*p*-C_6H_4Me	EtI	57	225	$C_{36}H_{33}N_2IS_3$	S, 11·4; I, 22·6	S, 11·5; I, 22·8
,, ...	,,	MeI	55	243	$C_{35}H_{33}N_2IS_3$	N, 5·2; I, 23·5	N, 5·15; I, 23·4
p-Xylyl ...	,,	EtI	47	168	$C_{38}H_{39}N_2IS_3$	I, 22·0	I, 21·75
,, ...	,,	MeI	45	230	$C_{38}H_{37}N_2IS_3$	I, 22·3	I, 22·3
β-$C_{10}H_7$ ...	,,	EtI	54	234	$C_{36}H_{28}N_2IS_3$	S, 10·6	S, 10·6

[a] Veratryl. [b] X = ·CMe_2·CH_2·CMe_3. [c] Ts = *p*-C_6H_4Me·SO_2. [d] Found: N, 5·3; S, 6·0; I, 24·4. Reqd.: N, 5·3; S, 6·0; I, 24·15%.

[1-*Methyl*-2-*quinoline*][3-*ethyl*-4 : 5-*diphenyl*-2-*thiazole*]*methincyanine iodide*, obtained similarly from 2-methyl-4 : 5-diphenylthiazole etho(ethyl sulphate) (1·2 g.), 2-methylthioquinoline methotoluene-*p*-sulphonate (1·0 g.) ethanol (10 c.c.), and triethylamine (0·5 c.c.), formed orange needles, m. p. 271°, from ethanol (Found: N, 5·0; I, 23·1. $C_{28}H_{25}N_2IS$ requires N, 5·1; I, 23·2%). $\lambda_{max.}$ 490 mμ in methanol.

[1-*Methyl*-2-*quinoline*][3-*ethyl*-4-p-*methoxyphenyl*-5-*phenyl*-2-*thiazole*]*methincyanine iodide* formed orange needles, m. p. 267°, from ethanol (Found: S, 5·5; I, 22·1. $C_{29}H_{27}ON_2IS$ requires S, 5·55; I, 22·0%). $\lambda_{max.}$ 490 mμ in methanol.

[1-*Methyl*-2-*quinoline*][3-*ethyl*-5-*phenoxy*-4-*phenyl*-2-*thiazole*]*methincyanine iodide* formed fine, orange threads, m. p. 258°, from ethanol (Found: S, 5·7; I, 22·3. $C_{28}H_{25}ON_2IS$ requires S, 5·7; I, 22·5%). $\lambda_{max.}$ 480 mμ in methanol.

[1-*Methyl*-2-*quinoline*][3-*ethyl*-5-*phenyl*-4-(3 : 4-*dimethoxyphenyl*)-2-*thiazole*]*methincyanine iodide* was obtained as flat, rust-red needles, m. p. 258°, from methanol (Found: I, 20·4. $C_{30}H_{29}O_2N_2IS$ requires I, 20·45%). $\lambda_{max.}$ 490 mμ in methanol.

[1-*Ethyl*-2-*quinoline*][2-*methyl*-4-*phenyl*-5-p-*tolylthio*-2-*thiazole*]*methincyanine iodide* formed flat, glossy, red needles, m. p. 227—228°, from methanol (Found: S, 10·4; I, 20·6. $C_{30}H_{27}N_2IS_2$ requires S, 10·55; I, 20·95%). $\lambda_{max.}$ 485 mμ in methanol.

Carbocyanines.—In all cases these were obtained by acetylating the required 2-2′-anilinovinyl derivative in acetic anhydride (½ hour's reflux), removing the solvent, and treating the resultant oily 2-2′-acetanilidovinyl derivative (1 mol.) with the parent 2-methylthiazolium salt (1 mol.) in presence of alcoholic triethylamine.

Bis-(3-*ethyl*-4 : 5-*diphenyl*-2-*thiazole*)*trimethincyanine iodide* was obtained as matted gold threads, m. p. 180°, from ethanol (Found: S, 9·1; I, 18·1. $C_{37}H_{33}N_2IS_2$ requires S, 9·2; I, 18·25%). $\lambda_{max.}$ 588 mμ in methanol.

Bis-(3-*ethyl*-4-p-*methoxyphenyl*-5-*phenyl*-2-*thiazole*)*trimethincyanine iodide* formed purple threads, m. p. 181°, from methanol (Found: I, 17·1. $C_{39}H_{37}O_2N_2IS_2$ requires I, 16·8%). $\lambda_{max.}$ 590 mμ in methanol.

Bis-[3-*ethyl*-4-p-*methoxyphenyl*-5-*phenyl*-2-*thiazole*]-β-*methyltrimethincyanine iodide* formed green crystals, m. p. 249°, from ethanol (Found: I, 16·4. $C_{40}H_{39}O_2N_2IS_2$ requires I, 16·5%). $\lambda_{max.}$ 561 mμ in methanol.

Bis-(3-*ethyl*-4-(3 : 4-*dimethoxyphenyl*)-5-*phenyl*-2-*thiazole*)*trimethincyanine iodide* was obtained as brilliant green crystals, m. p. 179°, from methanol (Found: S, 7·6; I, 15·4. $C_{41}H_{41}O_4N_2IS_2$ requires S, 7·85; I, 15·6%). $\lambda_{max.}$ 590 mμ in methanol.

Bis-(3-*ethyl*-5-*phenyl*-4-p-*xylyl*-2-*thiazole*)*trimethincyanine perchlorate* formed a mauve crystalline powder, m. p. 225°, from ethanol (Found: N, 3·8; S, 8·7. $C_{41}H_{41}O_4N_2ClS_2$ requires N, 3·85; S, 8·85%). $\lambda_{max.}$ 592 mμ in methanol.

Bis-(4-p-*methoxyphenyl*-3-*methyl*-5-*phenoxy*-2-*thiazole*)*trimethincyanine perchlorate* formed a bronze crystalline powder, m. p. 240°, from methanol (Found: C, 60·5; H, 4·5; S, 8·7. $C_{37}H_{33}O_6N_2ClS_2$ requires C, 60·5; H, 4·5; S, 8·75). $\lambda_{max.}$ 580 mμ in methanol.

Bis-(3-*methyl*-4-*phenyl*-5-p-*tolylthio*-2-*thiazole*)*trimethincyanine iodide* was obtained as flat,

bronze needles, m. p. 224°, from ethanol (Found : S, 17·05. $C_{37}H_{33}N_3IS_4$ requires S, 16·85%). $\lambda_{max.}$ 585 mμ in methanol.

Bis-(3-ethyl-4-β-naphthyl-5-p-tolylthio-2-thiazole)trimethincyanine iodide formed bronze crystals, m. p. 194°, from methanol (Found : S, 14·2; I, 14·3. $C_{47}H_{41}N_3IS_4$ requires S, 14·4; I, 14·3%). $\lambda_{max.}$ 585 mμ in methanol.

[3-Ethyl-2-benzothiazole][3-ethyl-4-β-naphthyl-5-p-tolylthio-2-thiazole]trimethincyanine perchlorate formed green prisms, m. p. 205°, from methanol (Found : S, 14·4. $C_{34}H_{31}O_4N_2ClS_3$ requires S, 14·5%) $\lambda_{max.}$ 565 mμ in methanol.

[3-Ethyl-2-benzothiazole][3-ethyl-4-phenyl-5-p-tolylthio-2-thiazole]trimethincyanine iodide formed soft, flat, bronze needles, m. p. 195°, from methanol (Found : S, 15·1; I, 19·7. $C_{30}H_{29}N_3IS_3$ requires S, 15·0; I, 19·85%). $\lambda_{max.}$ 560 mμ in methanol.

*Dimethin*merocyanines.—These dyes are derived from 3-ethyl-2-thiothiazolid-4-one (3-ethylrhodanine) (VI) or 2-ethylthiothiazol-5-one (VII). They were obtained by standard procedures through the 2-2′-acetanilidovinyl derivative of the quaternized thiazole and ketomethylene compound or from the 2-methyl derivative of the quaternized thiazole and 4-ethoxymethylene-2-ethylthiothiazol-5-one (cf. Cook, Harris, and Shaw, *J.*, 1949, 1435; Aubert, Knott, and Williams, *J.*, 1951, 2185). Unless otherwise stated, the *dyes* were recrystallized from benzene or benzene–methanol, usually forming needles : see Tables 7 and 8.

TABLE 7. *3-Ethyl-5-(G-thiazolin-2-ylidene-ethylidene)-2-thiothiazolid-4-ones* (VI).

Substituent G	Appearance	M. p.	$\lambda_{max.}$ (mμ) (MeOH)	Formula	Found, % N	Found, % S	Required, % N	Required, % S
3-Ethyl-4 : 5-diphenyl-	Magenta	242°	550	$C_{24}H_{22}ON_2S_3$	6·2	21·2	6·25	21·35
4-*p*-Methoxyphenyl-3-methyl-5-phenyl-	Red	216	552	$C_{24}H_{22}O_2N_2S_3$	—	20·1	—	20·4
3-Ethyl-4-*p*-methoxyphenyl-5-phenyl-	Red	197	548	$C_{25}H_{24}O_2N_2S_3$	—	19·6	—	19·85
4-(3 : 4-Dimethoxyphenyl)-3-ethyl-5-phenyl-	Green	199	554	$C_{26}H_{26}O_3N_2S_3$ [a]	5·5	18·5	5·5	18·8
3-Methyl-5-phenyl-4-*p*-xylyl-	Green	111	552	$C_{25}H_{24}ON_2S_3$	—	20·6	—	20·7
3-Ethyl-5-phenyl-4-*p*-xylyl-	Green-brown	190	554	$C_{26}H_{26}ON_2S_3$	—	20·15	—	20·1
3-Ethyl-5-phenoxy-4-phenyl-	Green	174	544	$C_{24}H_{22}O_2N_2S_3$	5·7	20·3	6·0	20·6
4-*p*-Methoxyphenyl-3-methyl-5-phenoxy-	Green	186	547	$C_{24}H_{22}O_3N_2S_3$	5·85	19·6	5·8	19·9
3-Ethyl-4-*p*-methoxyphenyl-5-phenoxy-	Purple	150	544	$C_{25}H_{24}O_3N_2S_3$	—	19·2	—	19·35
4-*p*-Methoxyphenyl-3-methyl-5-(1 : 1 : 3 : 3-tetramethylbutyl)phenoxy-	Dull red	161	546	$C_{32}H_{38}O_3N_2S_3$ [b]	—	16·3	—	16·15
3-Ethyl-4-phenyl-5-*p*-tolylthio-	Bronze	165	544	$C_{25}H_{24}ON_2S_4$	—	25·6	—	25·8
3-Ethyl-4-β-naphthyl-5-*p*-tolylthio-	Garnet	198	544	$C_{29}H_{26}ON_2S_4$	5·1	23·6	5·15	23·4
3-Ethyl-4-*p*-methoxyphenyl-	Red	225	540	$C_{19}H_{19}O_2N_2S_3$	6·9	23·6	6·95	23·8

[a] Found : C, 61·3; H, 5·05. Reqd. : C, 61·2; H, 5·1%. [b] Found : C, 64·2; H, 6·3. Reqd. : C, 64·7; H, 6·4%.

TABLE 8. *2-Ethylthio-4-(G-thiazolin-2-ylidene-ethylidene)thiazol-5-ones* (VII).

Substituent G	Appearance	M. p.	$\lambda_{max.}$ (mμ) (MeOH)	Formula	Found, % N	Found, % S	Required, % N	Required, % S
3-Ethyl-4 : 5-diphenyl-	Violet	208°	547	$C_{24}H_{22}ON_2S_3$	6·3	21·5	6·25	21·35
3-Ethyl-4-*p*-methoxyphenyl-5-phenyl-	Purple	181	548	$C_{25}H_{24}O_2N_2S_3$	—	19·8	—	20·0
4-(3 : 4-Dimethoxyphenyl)-3-ethyl-5-phenyl-	Red	229	550	$C_{26}H_{26}O_3N_2S_3$	5·7	19·0	5·5	18·8
3-Methyl-5-phenyl-4-*p*-xylyl-	Steel grey-red	108	548	$C_{25}H_{24}ON_2S_3$	5·85	20·5	6·05	20·7
4-*p*-Methoxyphenyl-3-methyl-5-phenoxy-	Red, green reflex	168	543	$C_{24}H_{22}O_3N_2S_3$	5·6	20·1	5·8	19·9
3-Ethyl-4-*p*-methoxyphenyl-5-phenoxy-	Purple	164	542	$C_{25}H_{24}O_3N_2S_3$	5·35	19·3	5·65	19·35
3-Methyl-4-phenyl-5-*p*-tolylthio-	Blue-green	133	544	$C_{24}H_{22}ON_2S$	5·8	26·7	5·8	26·8
3-Methyl-4-β-naphthyl-5-*p*-tolylthio-	Violet	180	544	$C_{28}H_{24}ON_2S_4$	—	24·1	—	24·0
3-Ethyl-4-*p*-methoxyphenyl-(X)	Maroon	182	527	$C_{19}H_{19}O_2N_2S_3$	6·75	23·7	6·95	23·8

3-Ethyl-5-(3-ethyl-4-p-methoxyphenyl-5-phenylthiazolin-2-ylideneisopropylidene)-2-thiothiazolid-4-one.—2-2′-Anilinopropenyl-4-*p*-methoxyphenyl-5-phenylthiazole ethiodide (4 g.) and acetic anhydride (20 c.c.) were refluxed for 30 minutes and the solvents removed. 3-Ethylrhodanine (1·2 g.), ethanol (10 c.c.), and triethylamine (1·5 c.c.) were added and the whole refluxed for 10 minutes. The dye (1·65 g.) crystallized on chilling and formed violet needles, m. p. 168°, from benzene–light petroleum (Found: N, 5·65; S, 19·5. $C_{26}H_{26}O_2N_2S_3$ requires N, 5·65; S, 19·4%). $\lambda_{max.}$ 535 mμ in methanol.

4-(3-Ethyl-4-p-methoxyphenyl-5-phenylthiazolin-2-ylideneisopropylidene)-2-ethylthiothiazol-5-one formed violet needles, m. p. 236°, from benzene–methanol (Found: N, 5·4; S, 19·4. $C_{26}H_{26}O_2N_2S_3$ requires N, 5·65; S, 19·4%). $\lambda_{max.}$ 550 mμ in methanol.

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788. *Titanium Tetrachloride as a Catalyst in the Friedel–Crafts Reaction. Part II.* Addition Compounds.*

By N. M. CULLINANE, S. J. CHARD, and D. M. LEYSHON.

Titanium tetrachloride combines with acid chlorides, forming solid complexes of the general formula $TiCl_4$,R·COCl. In some cases the results have been confirmed by thermal analysis. Similar products are formed by ketones and by anisole.

Thermal analysis indicates that the titanic salt forms with benzene the complex $3TiCl_4,C_6H_6$.

IN Friedel–Crafts syntheses additive compounds derived from aluminium chloride and organic molecules have been frequently obtained. In the acylation processes already described (Cullinane, Chard, and Leyshon, Part I*), formation of compounds of similar types with titanium tetrachloride in place of aluminium chloride was also observed, and some examples of these are described in the present memoir.

A number of such complexes of titanic chloride have been previously reported; solid products have been isolated with nitro-compounds (cf. Hertel and Demmer, *Annalen*, 1932, **499**, 134; Reihlen and Hake, *Annalen*, 1927, **452**, 47; Pushin *et al.*, *ibid.*, 1942, **551**, 259; Hertel, *ibid.*, 1942, **553**, 286), nitroso-compounds (Reihlen and Hake, *loc. cit.*), nitriles (Hertel and Demmer, *loc. cit.*; Ulich, Hertel, and Nespital, *Z. physikal. Chem.*, 1932, *B*, **17**, 21; Pushin *et al.*, *Annalen*, 1942, **553**, 278), aldehydes (Scagliarini and Tartarini, *Atti R. Accad. Lincei*, 1926, **4**, 318), ethers (Demetrios and Ladikos, *Praktika Akad. Athenon*, 1930, **5**, 449), indoles (Schmidtz-Dumont and Motzkus, *Ber.*, 1929, **62**, 466).

Complexes prepared by the present authors include those formed by acid chlorides (cf. Bertrand, *Bull. Soc. chim.*, 1880, **33**, 403; 1881, **34**, 631); all were of the composition $TiCl_4$,R·COCl and their constitutions were confirmed in some cases by means of temperature–concentration diagrams.

Complexes with acetic or benzoic anhydride could not be obtained pure, probably because these substances react to some extent with the titanium halide forming the corresponding acid chlorides; a similar reaction takes place between aluminium chloride and acetic anhydride, as noted by Groggins and Nagel (*Ind. Eng. Chem.*, 1934, **26**, 1313; cf. Adrianowsky (*Bull. Soc. chim.*, 1879, **31**, 199). Scagliarini and Tartarini (*loc. cit.*; cf. Evard, *Compt. rend.*, 1933, **196**, 2007) obtained from titanium tetrachloride and benzophenone a product to which they assigned the formula $TiCl_4$, $COPh_2$, and Hertel and Demmer (*loc. cit.*) claimed to have prepared also the compound $TiCl_4,2COPh_2$. In the present work

* Part I, *J.*, 1952, 376.

we have isolated solid complexes of titanic chloride with *p*-methoxyacetophenone, acetophenone, and methyl, ethyl, and *n*-propyl *p*-tolyl ketone; all of these were 1 : 1 products.

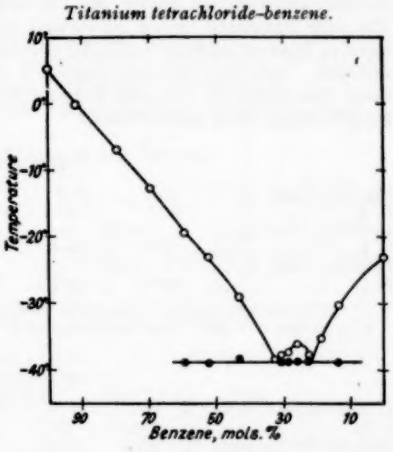
A well-defined compound $TiCl_4$,PhOMe was obtained from anisole. The product formed with benzene had a low freezing point and was therefore subjected to thermal analysis (Figure); its composition corresponding to $3TiCl_4,C_6H_6$.

Experimental.

In all our experiments great care was taken to exclude moisture since all the products were hydrolysed at once by water.

Materials.—Titanium tetrachloride was boiled under reflux over copper turnings for 4 hours and then distilled, giving a water-white fraction, b. p. 136°.

" AnalaR " carbon disulphide was dried ($CaCl_2$) and fractionated; " thiophen-free " benzene and sulphur-free toluene were dried over sodium and distilled. The acid chlorides were boiled under reflux for an hour and then fractionated. " AnalaR " acetic anhydride was redistilled; benzoic anhydride, recrystallised from benzene–light petroleum, had m. p. 42°. Acetophenone (from B. D. H.) was dried ($CaCl_2$) and fractionated, then having m. p. 20°. Methyl (b. p. 224°), ethyl (b. p. 233°), and *n*-propyl (b. p. 250°) *p*-tolyl ketones (cf. Cullinane, Chard, and Leyshon, *loc. cit.*) were similarly treated. *p*-Methoxyacetophenone (m. p. 38°) and *p*-methoxybenzophenone (m. p. 62°) were recrystallised from alcohol and dried in a desiccator over phosphoric oxide.



Titanium was determined in the complexes by precipitation with ammonia solution and ignition to the dioxide, and chloride by precipitation with silver nitrate (cf. Cullinane *et al.*, *J. Soc. Chem. Ind.*, 1950, **69**, S 38).

Addition Compounds with Acid Chlorides.—In general the acid chloride was dissolved in dry carbondisulphide, and a solution containing an approximately equivalent amount of the titanium halide in the same solvent added. The precipitated complex was dissolved by careful heating, the solution cooled, and the supernatant liquid decanted from the crystals, which were washed with a little carbon disulphide and dried. With *n*- and *iso*-butyryl chlorides the procedure was modified somewhat; approximately equimolecular quantities of titanic chloride and acid chloride were mixed and placed in an ice-salt bath until partial solidification occurred, the mother-liquor was poured off, and the crystals were washed with a little cooled carbon disulphide, dried, and analysed. The following results were obtained: Titanium tetrachloride–acetyl chloride, small yellow plates, m. p. 19—20° (Found: Ti, 18·1; Cl 66·1. Calc. for $TiCl_4,CH_3{\cdot}COCl$: Ti, 17·9; Cl, 66·1%). Bertrand (*loc. cit.*) gives m. p. 25—30°.

Titanium tetrachloride–propionyl chloride, yellow prisms, m. p. 28·5° (Found: Ti, 16·9; Cl, 63·6. $TiCl_4,C_2H_5{\cdot}COCl$ requires Ti, 17·0; Cl, 62·9%).

Titanium tetrachloride–n-butyryl chloride, yellow needles, m. p. −4° (Found: Ti, 16·0; Cl, 59·7. $TiCl_4,C_3H_7{\cdot}COCl$ requires Ti, 16·2; Cl, 59·9%).

Titanium tetrachloride–isobutyryl chloride, yellow prisms, m. p. 11° (Found: Ti, 16·6; Cl, 59·6%).

Titanium tetrachloride–benzoyl chloride, small yellow needles, m. p. 63° (Found: Ti, 14·4; Cl, 53·9. Calc. for $TiCl_4,C_6H_5{\cdot}COCl$: Ti, 14·5; Cl, 53·7%). Bertrand (*loc. cit.*) gives m. p. 65°.

Addition Compounds with Ketones.—In the normal procedure an approximately equivalent amount of the titanium salt dissolved in toluene was added to a similar solution of the ketone. Finely divided crystals were gradually deposited at room temperature, and these were washed with a little toluene and dried.

Titanium tetrachloride–acetophenone, bright-yellow crystals which slowly darkened when heated and decomposed at 137—139° (Found: Ti, 16·0; Cl, 45·3. $TiCl_4,C_6H_5{\cdot}CO{\cdot}CH_3$ requires Ti, 15·7; Cl, 45·8%).

Titanium tetrachloride–methyl p-*tolyl ketone*, yellow needles, which darkened on heating and decomposed at about 120° (Found: Ti, 14·5; Cl, 43·4. $TiCl_4,CH_3{\cdot}C_6H_4{\cdot}CO{\cdot}CH_3$ requires Ti, 14·8; Cl, 43·8%).

Titanium tetrachloride–ethyl p-*tolyl ketone*, orange plates, m. p. 65° (Found: Ti, 13·7; Cl, 41·4. $TiCl_4,CH_3{\cdot}C_6H_4{\cdot}CO{\cdot}C_2H_5$ requires Ti, 14·2; Cl, 42·0%).

*Titanium tetrachloride–*n-*propyl* p-*tolyl ketone*, bright yellow needles, darkening when heated and decomposing at about 110° (Found: Ti, 13·4; Cl, 39·8. $TiCl_4,CH_3{\cdot}C_6H_4{\cdot}CO{\cdot}C_3H_7$ requires Ti, 13·6; Cl, 40·3%).

*Titanium tetrachloride–*p-*methoxyacetophenone*, scarlet prisms, which darkened on heating and melted at 133° to a dark liquid which decomposed on further heating (Found: Ti, 14·6; Cl, 42·3. $TiCl_4,CH_3O{\cdot}C_6H_4{\cdot}CO{\cdot}CH_3$ requires Ti, 14·1; Cl, 41·7%).

Other ketones gave reddish oils at the ordinary temperatures.

Titanium tetrachloride–Anisole.—The dark-red solution obtained by mixing the components in benzene deposited the *complex* as reddish-orange plates which were recrystallised from the same solvent and had m. p. 36° (Found: Ti, 15·8; Cl, 47·7. $TiCl_4,C_6H_5{\cdot}OCH_3$ requires Ti, 16·1; Cl, 47·6%).

Thermal Analyses.—In certain cases thermometric analyses were carried out by the cooling curve method. The apparatus consisted of a jacketed tube into which the components were distilled immediately before use, all essential precautions being taken to exclude moisture. The tube was fitted with a stirrer and immersed in a suitable bath; for lower temperatures a freezing mixture of ether and solid carbon dioxide contained in an unsilvered Dewar vessel was suitable. Temperatures were recorded on a standardized pentane thermometer. Fresh mixtures were made up for each freezing-point determination. The data are tabulated (eutectic temperatures are in parentheses).

Titanium tetrachloride–benzene.

Benzene, mols. % ...	100	91·9	79·5	69·6	59·5	52·2	
F. p.	5·5°	0·0°	−6·8°	−12·6°	−19·3° (−38·7°)	−23·0°	(−38·9°)
Benzene, mols. % ...	43·3	32·9	28·6	25·9			
F. p.	−29·0° (−38·4°)	−38·3°	−37·3° (−38·7°)	−36·0° (−38·7°)			
Benzene, mols. % ...	22·6	18·7	13·7	0			
F. p.	−37·7° (−38·7°)	−35·1° (−38·7°)	−30·2°	−23·1°			

The system indicates a compound $3TiCl_4,C_6H_6$, with a congruent m. p. of −36·0° and two eutectics both at about −38·7°, corresponding to 31·5 and 21·5 mols. % of benzene respectively.

Titanium tetrachloride–acetyl chloride.

Acetyl chloride, mols. %	100	97·1	93·7	85·3	79·5	63·4	53·0	42·7
F. p.	−112°	−28·1°	−7·0°	8·8°	15·1°	18·5°	19·3°	19·1°
Acetyl chloride, mols. %	33·3	22·5	15·5	6·6	4·7	0·0		
F. p.	18·3°	15·1°	11·9° (−28·4°)	2·1° (−28·6°)	−0·8°	−23·1°		

The system reveals a compound $TiCl_4,CH_3{\cdot}COCl$, with a congruent m. p. of 19·3°. One eutectic was at −28·5°, corresponding to 1·3 mols. % of acetyl chloride, the other was too low to be determined

Titanium tetrachloride–benzoyl chloride.

Benzoyl chloride, mols. %	100	97·4		95·5		86·3	82·4	67·6
F. p.	−1·2°	−3·5°	(−3·8°)	1·1°	(−4·0°)	36·5°	47·1°	56·6°
Benzoyl chloride, mols. %	52·3	39·8	27·2	18·9	8·4	3·7	0·0	
F. p.	61·7°	62·4°	59·3°	56·2°	45·2°	35·0°	(−24·5°)	−23·1°

A compound $TiCl_4,C_6H_5{\cdot}COCl$ is indicated, its congruent m. p. being 62·5°. The eutectics were at −3·9° and −24·5°, corresponding to 98 and 1 mol. % of benzoyl chloride respectively.

We thank Messrs. Peter Spence and Sons, Ltd., for gifts of titanium tetrachloride and the Department of Scientific and Industrial Research for a Maintenance Grant to one of us (D. M. L.).

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CARDIFF.

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789. *Heterocyclic Syntheses with Malonyl Chloride. Part I. Pyrano-1 : 3-dioxins from Ketones.*

By S. J. Davis and J. A. Elvidge.

The vigorous reaction between malonyl chloride and acetone has been reinvestigated and found not to yield phloroglucinol as hitherto claimed. The reaction is general for ketones and yields 2 : 2-disubstituted derivatives of 6′-chloro-2′ : 4-diketopyrano(3′ : 4′-5 : 6)-1 : 3-dioxin, a new unsaturated hetero-dicyclic system. Structural evidence for the products is presented and their formation discussed.

According to Komninos (*Compt. rend.*, 1918, **167**, 781; *Bull. Soc. chim.*, 1918, **23**, 449) malonyl chloride and acetone react vigorously in the presence of marble, to give phloroglucinol and a red product (decomp. 160°), claimed to be 3 : 5-diketohexanoyl chloride,* Cl·CO·CH_2·CO·CH_2·COMe, convertible into phloroglucinol by carbonate and hot water. Reinvestigation has shown that neither compound is formed;† the product is a chloropyrono-1 : 3-dioxin (III; R = R′ = Me).

We found that the reaction affords a colourless compound (I) (decomp. 183°), $C_9H_7O_5Cl$, which could not be converted into phloroglucinol. The compound was neutral but reacted slowly with cold water and alcohol to give acid solutions which gave red colours with ferric chloride. Ketones other than acetone yielded similar chloro-products, listed in Table 1.

Table 1. *Products from malonyl chloride and ketones.*

Ketone	Product	M. p.	Light absorption in dioxan $\lambda_{max.}$ (Å)	ϵ
$COMe_2$	$C_9H_7O_5Cl$ (I)	183° †	3020 *	9,700
			3140	10,900
			3180 *	9,700
$COPh_2$	$C_{19}H_{11}O_5Cl$ (II)	179 †	2450 *	14,200
			2510	16,700
			2580	15,300
			2900 *	7,100
			3040	8,200
			3120 *	7,100
COPhMe	$C_{14}H_9O_5Cl$	147	2800	4,700
			3140	10,000
$COMePr^n$	$C_{11}H_{11}O_5Cl$	89°	3140	8000
$COEt_2$	$C_{11}H_{11}O_5Cl$	104	—	—
*cyclo*Hexanone	$C_{12}H_{11}O_5Cl$	129	—	—
CH_2·CO·CH_2·CO_2Et	$C_{12}H_{11}O_7Cl$	118 †	—	—
CH_2·CO·CO_2Et	$C_{11}H_9O_7Cl$	87·5	—	—

* Inflection.
† With decomp.

These have a characteristic absorption band at *ca.* 3140 Å. Their formation may be represented: $RR'CO + 2CH_2(COCl)_2 = RR'C_7HO_5Cl + 3HCl$. The reaction with benzophenone shows that only the CO group of the ketone is involved.

Treatment of the benzophenone compound (II) with boiling ethanol and then with ammonia in the cold gave benzophenone and malonamide. With boiling water, carbon dioxide (83% of 3 mols.), hydrogen chloride (1 mol.), benzophenone (1 mol.), and acetone (as the 2 : 4-dinitrophenylhydrazone) were obtained, as shown by the equation

$$C_{19}H_{11}O_5Cl + 3H_2O = Ph_2CO + HCl + 3CO_2 + Me_2CO$$

The formation of acetone and carbon dioxide suggested that the molecule of the chloro-compound contained a bismalonyl residue, *i.e.*, a potential acetonetricarboxylic grouping.

The benzophenone compound (II) was then heated for a short time with three mols. of ethanol. Hydrogen chloride was evolved and, from the residue, which contained benzophenone and gave a red colour with ferric chloride, a crystalline copper derivative was

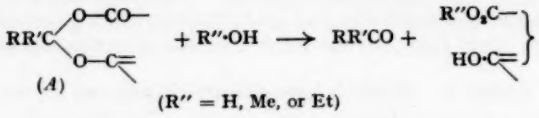
* Geneva nomenclature, CO_2H = 1.

† References to the reaction as a synthesis of phloroglucinol (*e.g.*, Beilstein's "Handbuch, etc.," 4th Edn., 1st Ergänzungsband, Vol. VI, p. 545; Richter, "The Chemistry of the Carbon Compounds," Elsevier, New York, 1946, Vol. III, p. 230; Bernthsen, "A Textbook of Organic Chemistry," Blackie and Son, Glasgow, 1942, p. 403) consequently need revision.

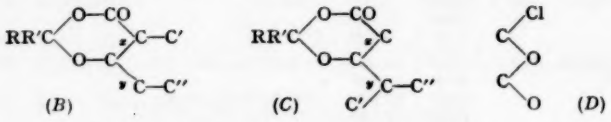
prepared. This was identical with the copper enolate of triethyl acetone-1 : 1 : 3-tricarboxylate, synthesised unambiguously *via* the reaction of malonic monoethyl ester chloride with ethyl magnesiomalonate. Similar degradation of the acetone-derived chloro-compound (I) with boiling ethanol led to the same copper derivative.

The benzophenone compound (II) in dioxan reacted with cold water, yielding benzophenone and a crystalline water-soluble acid, in accordance with the equation $C_{19}H_{11}O_5Cl + H_2O = Ph_2CO + C_6H_3O_5Cl$. The acid, which gave a deep red colour with ferric chloride, was evidently the source of the smaller fragments obtained in the reaction of (II) with hot water. With methanol and ethanol in dioxan in the cold, (II) underwent fissions to benzophenone and crystalline enolic products, $C_7H_5O_5Cl$ and $C_8H_7O_5Cl$, respectively, which were probably the methyl and ethyl esters of the acid. On attempted hydrolysis of the ethyl compound with one equivalent of sodium hydroxide, carbon dioxide was evolved, and from the solution ethyl acetoacetate was isolated as the 2 : 4-dinitrophenylhydrazone. Reaction of the acid with diazomethane, in an attempt to obtain its methyl ester, yielded a chlorine-free enolic product, $C_8H_8O_6$. However, an identical compound was formed from the methyl compound $C_8H_7O_5Cl$ and diazomethane, and so the suspected connection between the water and the methanol product was established.

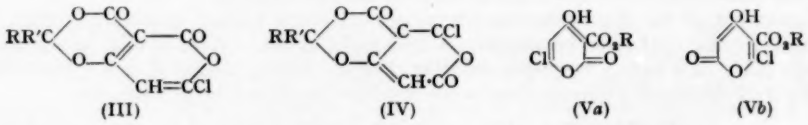
The fission of the benzophenone compound (II) to these products could be explained thus :



and there were two ways, (*B*) and (*C*), in which the C_6-acetone-1 : 1 : 3-tricarboxylic residue could be linked to the ketone moiety as in (*A*). One of the linkings *x* and *y* was necessarily



a double bond. Atoms Cl, H, and 2O had still to be accommodated so as to indicate that the chlorine atom was less reactive than in a COCl group and that positions C′ and C″ were potential carboxyl groups. The arrangement (*D*) satisfactorily met these requirements and could be accommodated best on skeleton (*B*); (*C*) leads to a four-membered ring structure. Hence the possible formulæ for the malonyl chloride–ketone products were reduced to (III) and (IV).



It followed that the acid degradation product and its methyl and ethyl esters were (V*a* or *b*; R = H, Me, and Et).

The related pyrones (VI) of established constitution (Staudinger and Becker, *Ber.*, **1917**, **50**, 1016) were found to have light-absorption spectra similar to those of the acid and its esters (see Table 2), which confirmed the pyrone structures. Reaction of the methyl chloro-ester with sodium methoxide gave a crystalline methoxy-derivative, $C_7H_5O_5$·OMe, identical with the pyrone (VI; R = Me). Hence the degradation products were 6-chloro-4-hydroxy-2-pyrone-3-carboxylic acid derivatives (V*a*; R = H, Me, and Et). [The compound $C_8H_8O_6$ obtained by diazomethane, and isomeric with (VI; R = Me) was most probably the 6-hydroxymethyl derivative (VII).] It followed that the malonyl chloride–

ketone products (Table 1) had the structure (III). The compounds were 2 : 2-disubstituted derivatives of 6′-chloro-2′ : 4-diketopyrano(3′ : 4′-5 : 6)-1 : 3-dioxin.

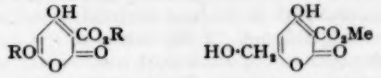
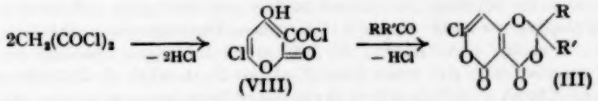


TABLE 2. *Light absorption of pyrone derivatives in dioxan.*

	Compound		$\lambda_{max.}$ (Å)	ϵ
(VI)	(synthesised by Staudinger's method)	R = Me	3050	18,400
		R = Et	3040	15,500
	[from degradation of (II)]	R = H	2950 *	8,600
			3040	10,100
(V*a*)		R = Me	3040	12,300
		R = Et	3040	11,500
			3190 *	10,500
(VI)	[from degradation of (II)]	R = Me	3040	17,600

* Inflection.

The following scheme is proposed, to account for the production of the pyrono-1 : 3-dioxins :



The first stage is a self-condensation of malonyl chloride (not hitherto demonstrated), induced by the ketone as a very weak base [cf. the formation of the pyrones (VI)]. Evidence for this was obtained by treating malonyl chloride with a non-reactive base of comparable strength (see Braude, *J.*, 1948, 1971). The effect of dioxan is shown in Table 3. The appearance of the characteristic absorption band at 3040 Å indicates that a pyrone, presumably (VIII), is formed quite rapidly at room temperature. (Stronger bases, *e.g.*, tertiary amines, react vigorously with malonyl chloride, producing dark tars.)

TABLE 3. *Light absorption of solutions of malonyl chloride.*

Solvent (dry)	*c* (% w/v)	Time (hrs.)	$\lambda_{max.}$ (Å)	$E^{1\%}_{1\ cm.}$
Dioxan	0·618	1	2800	40
			2930	31
			3040	26
		25	3040 (only)	135
*cyclo*Hexane	0·496	—	End absorption only (no change with time)	

Alternative schemes can be formulated in which the first step is an addition of malonyl chloride to the ketone to yield a monoester chloride, $COCl{\cdot}CH_2{\cdot}CO_2{\cdot}CClRR'$ (cf. the action of carbonyl chloride or oxalyl chloride on keto-compounds; Staudinger, *Ber.*, 1909, **42**, 3966). The next stages, to yield (III), would involve condensation of this ester either with itself, followed by elimination of one ketone residue, or with malonyl chloride. These schemes seem unlikely because the first step would consume the ketone—*i.e.*, the proton acceptor—required to induce formation of the pyrone ring at a succeeding stage. Experiment shows that (III; R = R′ = Me) is formed in high yield from acetone with an excess of malonyl chloride. Spontaneous condensation of malonyl chloride or malonic monoester chloride has not been observed. These compounds appear to be stable for long periods.

No representatives of the unsaturated pyrano(3′ : 4′-5 : 6)-1 : 3-dioxin ring system have hitherto been described, although a few derivatives of the fully reduced system are known (Späth, Lorenz, and Freund, *Ber.*, 1943, **76**, 722; 1944, **77**, 354). The new system is highly reactive and is being further investigated, together with implications deriving from the proposed mode of formation.

EXPERIMENTAL

Reaction of Malonyl Chloride with Acetone.—(a) *Repetition of Komninos's experiments.* Malonyl chloride (8·6 g., 6 c.c.) and acetone ("AnalaR"; 3·5 g., 4·3 c.c.) were mixed and small marble chips (6 g.) added. When the evolution of heat and gas slackened, acetone (2 c.c.)

was added and the mixture kept overnight protected from atmospheric moisture. Extraction (3 times) with hot acetone afforded a product (pale yellow prisms; 3·2 g.), m. p. *ca.* 180° (decomp., with darkening from 135°), identical with that given by method (*b*), below.

The filtrate was made alkaline with 2N-sodium hydroxide and evaporated to dryness, and the residue extracted with boiling ethanol. Evaporation of the extract afforded a semi-solid residue, which yielded no phloroglucinol by treatment with water and ether.

The yellowish crystalline product (above) (3 g.), water (10 c.c.), and marble chips (5 g.) were warmed together on the steam-bath for 2 hours. The filtrate contained chloride ion, but gave no characteristic colours with ferric chloride or Brady's reagent. Evaporation of the filtrate to dryness left calcium salts, and no phloroglucinol was obtained by ether-extraction.

(b) *Modified procedure.* A mixture of acetone ("AnalaR"; 10 c.c.) and malonyl chloride (3·5 c.c.) was heated under reflux until solid appeared, then cooled and treated with dry ether. Recrystallisation of the golden tablets (2·6 g., 63%, based on malonyl chloride) from dry benzene afforded colourless prisms, m. p. 183° (decomp.), of *6′-chloro-2′ : 4-diketo-2 : 2-dimethylpyrano-(3′ : 4′-5 : 6)-1 : 3-dioxin* (I) [Found: C, 46·9; H, 3·4; Cl, 15·25%; *M* (cryoscopic in bromoform), 234. $C_9H_7O_5Cl$ requires C, 46·9; H, 3·1; Cl, 15·4%; *M*, 230·6]. The yield was increased by using equivalent amounts of the reactants, but the product was more highly coloured. The compound did not react with aqueous sodium hydrogen carbonate during 5 minutes and gave no colour with ferric chloride in aqueous ethanol. When kept at room temperature in ethanol, and in aqueous dioxan, the solutions developed acidity and then gave red ferric colours.

Reaction of Benzophenone with Malonyl Chloride.—Benzophenone (15·2 g.) and malonyl chloride (16·2 c.c., 2 mols.) were heated at 100° until hydrogen chloride evolution ceased. Trituration of the product with dry ether gave *6′-chloro-2′ : 4-diketo-2 : 2-diphenylpyrano(3′ : 4′-5 : 6)-1 : 3-dioxin* (II) (24·45 g., 82%), which crystallised from benzene as very pale buff needles, m. p. 179° (decomp.) [Found: C, 63·9; H, 3·3; Cl, 9·8%; *M* (cryoscopic in bromoform), 299. $C_{19}H_{11}O_5Cl$ requires C, 64·3; H, 3·1; Cl, 10·0%; *M*, 354·7]. A solution in aqueous ethanol gradually became acid and then gave a reddish-purple colour with ferric chloride.

Reaction of Other Ketones with Malonyl Chloride.—The products listed in the annexed Table were prepared as above.

No.	CO compound	Malonyl chloride (c.c.)	Product triturated with *	Pyrano(3′ : 4′-5 : 6)-1 : 3-dioxin	Yield (%)	Form and solvent *
1	CH_3·CO·CO_2Et (2·2 c.c.)	4	Et_2O	2-*Carbethoxy*-6′-*chloro*-2′ : 4-*diketo*-2-*methyl*-	48	CCl_4
2	CH_3·CO·CH_2·CO_2Et (2·5 c.c.)	4	,,	2-*Carbethoxymethyl*-6′-*chloro*-2′ : 4-*diketo*-2-*methyl*-	60	Needles, CCl_4
3	COMePr^n (2·24 c.c.)	4	Pet (b)	6′-*Chloro*-2′ : 4-*diketo*-2-*methyl*-2-n-*propyl*-	92	Leaflets, Pet (b)
4	$COEt_2$ (10 c.c.)	3·5 (+5 g. $CaCO_3$)	†	6′-*Chloro*-2 : 2-*diethyl*-2′ : 4-*diketo*-	32	Needles, Pet (a)
5	$COPh_2$Me (2·4 c.c.)	4	—	6′-*Chloro*-2′ : 4-*diketo*-2-*methyl*-2-*phenyl*-	62	Needles, CCl_4
6	*cyclo*Hexanone (2·1 c.c.)	3·9	Et_2O	6′-*Chloro*-2′ : 4-*diketo*-2-spirocyclo-*hexyl*-	53	Plates, CCl_4

* Pet = light petroleum, b. p. (a) 60—80°, (b) 80—100°.
† Product isolated by extraction with chloroform.

No.	M. p.	Formula	Found (%) C	H	Cl	Required (%) C	H	Cl
1	87·5°	$C_{11}H_9O_7Cl$	45·45	3·25	11·9	45·75	3·15	12·3
2	118	$C_{12}H_{11}O_7Cl$	47·55	3·8	11·85	47·6	3·65	11·7
3	89	$C_{11}H_{11}O_5Cl$	51·4	4·6	14·05	51·1	4·3	13·7
4	104	,,	50·7	4·3	13·8, 13·6	,,	,,	,,
5	147	$C_{14}H_9O_5Cl$	57·0	3·1	12·15	57·1	3·1	12·1
6	129	$C_{12}H_{11}O_5Cl$	53·2	4·5	13·6	53·2	4·1	13·1

Degradation of the Benzophenone Product.—(a) *With boiling ethanol.* (i) The compound (II) (1 g.) and ethanol (0·45 c.c.) were heated on the steam-bath till evolution of hydrogen chloride ceased. Ether and ammonia (*d* 0·88) were added, and the mixture was shaken and kept for 24 hours. On evaporation, the ethereal layer gave benzophenone, m. p. 43—44°, and the aqueous layer gave malonamide, which after recrystallisation from ethanol had m. p. 164° (Found: N, 27·15. Calc. for $C_3H_6O_2N_2$: N, 27·4%), undepressed by authentic material.

(ii) *Formation of triethyl acetonetricarboxylate.* The compound (II) (0·71 g.), dry dioxan (1 c.c.), and ethanol (0·345 c.c.) were heated together on the steam-bath for 10 minutes. The

solution was shaken with cupric acetate (0·2 g.) in water (10 c.c.), and then with light petroleum (b. p. 40—120°) to remove benzophenone. The aqueous layer was filtered and cooled; the pale green crystalline precipitate had m. p. 85° alone and in admixture with an authentic specimen of the hydrated copper enolate of triethyl acetone-1 : 1 : 3-tricarboxylate (m. p. 85°) (see below).

(b) *With cold ethanol.* The compound (II) (1 g.) was dissolved in chloroform, and ethanol (0·45 c.c.) added with stirring. Next day, the solution was clarified and evaporated under reduced pressure. The residue was stirred with light petroleum (b. p. 80—100°), and the mixture filtered (filtrate *P*). Crystallisation of the solid from light petroleum (b. p. 80—100°) afforded *ethyl 6-chloro-4-hydroxy-2-ketopyran-3-carboxylate* (V*a*; R = Et) (0·3 g.) as needles, m. p. 121° (Found: C, 43·2; H, 3·3; Cl, 15·9. $C_8H_7O_5Cl$ requires C, 43·95; H, 3·25; Cl, 16·2%). In aqueous dioxan a deep reddish-purple colour was given with ferric chloride. Evaporation of filtrate *P* yielded benzophenone, m. p. *ca.* 40°, which was characterised as the 2 : 4-dinitrophenylhydrazone, m. p. 234°, undepressed by an authentic specimen.

On addition of the pyran (V*a*; R = Et) (0·68 g.) in dioxan (4 c.c.) to sodium hydroxide (0·25 g., 1 equiv.) in water (8 c.c.), there was a rapid evolution of carbon dioxide. After acidification with 2N-hydrochloric acid (3·1 c.c.) and addition of Brady's reagent, the 2 : 4-dinitrophenylhydrazone of ethyl acetoacetate was precipitated. This crystallised from ethanol and had m. p. 89°, undepressed by authentic material.

(c) *With boiling water.* The benzophenone compound (II) (340 mg.) and water (0·1 c.c.) were heated under reflux for 15 minutes. Gaseous acidic products were aspirated in a stream of dry, carbon dioxide-free nitrogen and absorbed in an excess of standard aqueous barium hydroxide. The evolved carbon dioxide (83·15% of 3 mols.) and hydrogen chloride (1·01 mol.) were estimated as barium carbonate and by back-titration of the barium hydroxide filtrate, respectively. The condenser was removed from the reaction vessel, which was then warmed in a current of nitrogen, and the gases were passed into Brady's reagent. Acetone 2 : 4-dinitrophenylhydrazone was precipitated, having m. p. 119·5°, undepressed by authentic material. The residue consisted of benzophenone (17·5 mg., 1·00 mol.), m. p. 35—40°; the 2 : 4-dinitrophenylhydrazone had m. p. 232°, undepressed by authentic material.

(d) *Reaction with cold water.* Compound (II) (1·42 g.) was dissolved in dry dioxan (25 c.c.) by heat, the solution cooled, and water (0·14 c.c.) added. Next day, the solution was concentrated to small bulk under reduced pressure and ether was added. The *6-chloro-4-hydroxy-2-ketopyran-3-carboxylic acid* (V*a*; R = H) (0·5 g.) crystallised as needles, m. p. 134·5°, from light petroleum (b. p. 80—100°) (Found: C, 38·2; H, 1·95; Cl, 18·75. $C_6H_3O_5Cl$ requires C, 37·85; H, 1·6; Cl, 18·6%). It gave a deep red colour with ferric chloride, and dissolved with effervescence in aqueous ammonium hydrogen carbonate.

(e) *Reaction with methanol.* The compound (II) (7·6 g.), dissolved in dioxan by heat, was treated in the cold with methanol (1·6 c.c.). Next day, the solution was evaporated to small bulk, and light petroleum (b. p. 60—80°) and ether were added. From benzene, the *methyl* ester (V*a*; R = Me) (3·7 g., 90%) separated as needles, m. p. 149° (Found: C, 41·45; H, 2·8; Cl, 17·05. $C_7H_5O_5Cl$ requires C, 41·1; H, 2·4; Cl, 17·35%). In aqueous dioxan a deep red colour was given with ferric chloride.

Methyl 4-Hydroxy-6-hydroxymethyl-2-ketopyran-3-carboxylate.—(i) To 6-chloro-4-hydroxy-2-ketopyran-3-carboxylic acid (320 mg.) in dioxan, a solution of diazomethane in ether (undried) was added in portions until gas evolution ceased. Evaporation, and trituration of the residue with light petroleum (b. p. 40—60°), gave a chlorine- and nitrogen-free product (Lassaigne's test), which gave a deep red colour with ferric chloride. The *methyl 4-hydroxy-6-hydroxymethyl-2-ketopyran-3-carboxylate* (50 mg.) had m. p. 147° after recrystallisation from benzene (Found: C, 48·1; H, 4·4. $C_8H_8O_6$ requires C, 48·0; H, 4·05%). A mixture with methyl 4-hydroxy-2-keto-6-methoxypyran-3-carboxylate (m. p. 149°) (below) had m. p. 120—122°.

(ii) Similarly, methyl 6-chloro-4-hydroxy-2-ketopyran-3-carboxylate (300 mg.) in dioxan with ethereal diazomethane (undried) afforded the 6-hydroxymethyl product (50 mg.), m. p. and mixed m. p. 147°.

Conversion of Methyl 6-Chloro-4-hydroxy-2-ketopyran-3-carboxylate into the 6-Methoxy-derivative with Sodium Methoxide.—Sodium (0·15 g.), dissolved in methanol (several c.c.), was added, during 5 minutes, to the pure chloro-pyran (0·65 g.) in dioxan (50 c.c.), with cooling. A precipitate formed at once. After 30 minutes, the mixture was just acidified with dilute sulphuric acid (*ca.* 50 c.c.), and the solution extracted with ether (50 + 25 c.c.). The combined extracts were dried (Na_2SO_4) and then evaporated under reduced pressure. From benzene–light petroleum (b. p. 60—80°), colourless halogen-free needles separated (90 mg.), which had m. p. 148·5° depressed to 120° by the starting material (Found: C, 47·8; H, 4·1. Calc. for

$C_8H_8O_6$: C, 48·0; H, 4·05%). The m. p. was not depressed by authentic methyl 4-hydroxy-2-keto-6-methoxypyran-3-carboxylate prepared by Staudinger and Becker's method (*loc. cit.*). The 6-methoxy-pyran gave an orange colour with ferric chloride in ethanol.

Degradation of the Acetone Compound with Ethanol.—The compound (I) (1 g.) was heated with ethanol (0·75 c.c.) on the steam-bath for 15 minutes. Hydrogen chloride was evolved. The resulting oil was kept under reduced pressure for several minutes, and then shaken with cupric acetate (0·4 g.) in water (10 c.c.). The pale green precipitate (1·3 g.; 98%) had m. p. 85° undepressed by an authentic specimen (see below) of the hydrated copper enolate of triethyl acetone-1 : 1 : 3-tricarboxylate.

Triethyl Acetone-1 : 1 : 3-tricarboxylate.—Malonic monoethyl ester chloride (42 g.) in dry ether (15 c.c.) and ethyl ethoxymagnesiomalonate [prepared from ethyl malonate (44·6 g.), according to Breslow, Baumgarten, and Hauser, *J. Amer. Chem. Soc.*, 1944, **66**, 1286] were heated under reflux for 30 minutes, then chilled and treated with an excess of dilute sulphuric acid. The *magnesium* derivative of triethyl acetone-1 : 1 : 3-tricarboxylate (18 g.), which separated, formed prismatic needles, m. p. 119°, from ethyl acetate (Found: Mg, 4·65. $C_{24}H_{34}O_{14}Mg$ requires Mg, 4·25%). The ethereal layer was combined with ethereal extracts (2 × 250 c.c.) of the aqueous phase, dried (Na_2SO_4), and evaporated. Ethyl malonate was removed under reduced pressure and the residue extracted with 5% sodium hydroxide solution. The extract was washed with ether and neutralised with dilute sulphuric acid, and the oily triethyl acetone-1 : 1 : 3-tricarboxylate (11·2 g.) isolated with chloroform. The pale green hydrated copper enolate, prepared from the ester according to Willstätter (*Ber.*, 1899, **32**, 1272), had m. p. 85°.

Analyses were performed in the micro-analytical laboratory (Mr. F. H. Oliver), and light absorption measurements in the spectrographic laboratory (Mrs. A. I. Boston) of this Department. We thank Professor R. P. Linstead, C.B.E., F.R.S., for his kind interest, and the Department of Scientific and Industrial Research for a maintenance grant (to S. J. D.).

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790. *The Hydrolysis of Aspirin in Guinea-pig Plasma.*

By L. J. Edwards.

The hydrolysis of aspirin has been measured in guinea-pig plasma at substrate concentrations of 10^{-2} to $2·5 \times 10^{-4}$M and plasma concentrations of 1% to 50%, a spectrophotometric method being used. The esterase-catalysed reaction is very much faster than the normal hydrolysis rate in a buffer at 37°, pH 7·4. Reaction velocity varies linearly with enzyme concentration at the higher concentrations; at lower concentrations there is a marked reduction in the relative activity. Activity is unchanged by storage for a week at 4° but is destroyed by 1 hour's heating at 57°. Calcium ions do not affect the reaction rate appreciably. Physostigmine retards the reaction only when present in relatively large doses at low plasma concentrations. It is estimated that the life of aspirin in the blood-stream would be between 5 and 10 minutes.

In earlier papers (Edwards, *Trans. Faraday Soc.*, 1950, **46**, 723; 1951, **47**, 1191; 1952, **48**, 696) the kinetics of hydrolysis and dissolution of aspirin in aqueous solution were studied at temperatures from 10° to 50° over the whole pH range, a spectrophotometric method being used for the simultaneous estimation of acetylsalicylic and salicylic acid.

The present study deals with measurements *in vitro* of the esterase-catalysed hydrolysis of aspirin in guinea-pig plasma at 37°, pH 7·4. Substrate concentrations from 10^{-2} to $2·5 \times 10^{-4}$M and plasma concentrations from 1% to 50% were investigated. These limits represent the extremes within which the reaction could be followed by the spectrophotometric technique with reasonable accuracy.

Experimental

The blood from each guinea-pig was collected, citrated, and centrifuged for 15 minutes to yield the plasma which, except where otherwise indicated, was used in the kinetic experiments within 30 minutes of the killing of the animal.

The aspirin, calcium aspirin, and physostigmine sulphate solutions were always freshly prepared immediately before a run, M/10-sodium citrate solution being used as solvent and adjusted to pH 7·4 whenever necessary before being mixed with the plasma. If further dilution of the reaction mixture was desired, the M/10-sodium citrate buffer was used. When physostigmine was used it was added to the plasma 30 minutes before addition of the substrate solution.

Reaction mixtures were placed in a thermostat at 37° and samples were withdrawn at intervals for spectrophotometric estimation by aid of the Hilger Medium Quartz instrument. Preliminary experiments, not reported here, established the approximate hydrolysis rates, and the sampling times were chosen accordingly to cover as much of the course of reaction as was practicable. In general, it was found that the hydrolysis of mixtures containing up to 20% of plasma could be followed by drawing samples from the thermostat bath as required, but for high plasma concentrations the reactions were carried out in quartz cells contained in a jacketed cell-holder described elsewhere (Edwards, *Chem. and Ind.*, 1952, 779). These fast reactions were followed by the fixed-density technique (*idem*, *Trans. Faraday Soc.*, 1950, **46**, 723; 1952, **48**, 696) in which the spectrophotometer is used as a transit instrument, a time base replacing the usual extinction base.

In estimations of the degree of hydrolysis the following extinction values at 296·5 mμ were used.

	ϵ		ϵ
Aspirin at pH 7·4 (fully ionized)	30	Physostigmine sulphate at pH 7·4	3000
Salicylic acid at pH 7·4 (fully ionized)	3520		

Plasma from :	$E^{10\%}_{1\,cm.}$	Plasma from :	$E^{10\%}_{1\,cm.}$
Guinea-pig no. 1	1·94	Guinea-pig no. 5 after 1 week in refrigerator	1·28
,, ,, 2	1·60	Guinea-pig no. 5 after 5 hours at 37°	1·29
,, ,, 3	2·00		
,, ,, 4	1·48		
,, ,, 5	1·28		

The density drum was calibrated against potassium chromate, $\epsilon_{max.}$ 4816 at 371 mμ being taken as standard.

Results.—The relevant experimental data and the observed velocity constants for each hydrolysis are set out in Tables 1 and 2. The constant $k_{obs.}$ is expressed in day^{-1} as in earlier papers.

TABLE 1. *Hydrolysis rates for aspirin in plasma at* 37°, pH 7·4.

Guinea-pig no.	Aspirin molarity	Plasma, vol. %	$k_{obs.}$	Guinea-pig no.	Aspirin molarity	Plasma, vol. %	$k_{obs.}$
—	10^{-2}	0	0·92	1	5×10^{-4}	2·5	13·6
—	5×10^{-3}	0	0·915	,,	$2·5 \times 10^{-4}$	2·5	12·4
—	5×10^{-4}	0	0·92	,,	10^{-2}	20	205
—	$2·5 \times 10^{-4}$	0	0·925	,,	5×10^{-3}	20	212
1	10^{-2}	2·5	14·8	,,	5×10^{-4}	20	185
,,	5×10^{-3}	2·5	14·8	,,	$2·5 \times 10^{-4}$	20	170

In the following expts. the aspirin molarity was 5×10^{-3}.

Guinea-pig no.	Plasma, vol. %	$k_{obs.}$	Guinea-pig no.	Plasma, vol. %	$k_{obs.}$	Guinea-pig no.	Plasma, vol. %	$k_{obs.}$
2	1	3·73	4 *	1	4·71	5 †	2·5	10·5
,,	2·5	9·74	,,	2·5	12·3	,,	5	25·1
,,	5	21·9	,,	5	27·2	,,	10	59·9
,,	10	49·1	,,	10	68·0			
,,	20	124	,,	20	162	5 ‡	2·5	0·93
,,	35	269	,,	35	321	,,	5	0·91
,,	50	400	,,	50	500	,,	10	0·93
						,,	20	0·985
3	1	6·22	5	2·5	10·0			
,,	2·5	16·0	,,	5	25·9			
,,	5	38·5	,,	10	61·4			
,,	10	91	,,	20	159			
,,	20	249	,,	35	328			
,,	35	450						

* Ca salt.
† Plasma kept for 1 week at 4° before use.
‡ Plasma heated at 57° for 1 hour before use.

The value of $k_{obs.}$ for the hydrolysis catalysed by the water and hydroxyl ion present was about 0·92 at all concentrations of substrate. This is in agreement with values already reported

TABLE 2. *Effect of physostigmine sulphate on esterase-catalysed hydrolysis of* 5×10^{-3}M-*aspirin at* 37°, pH 7·4.

Guinea-pig no.	Plasma, vol. %	Physostigmine molarity	$k_{obs.}$	Guinea-pig no.	Plasma, vol. %	Physostigmine molarity	$k_{obs.}$
2	1	0	3·73	2	5	0	21·9
,,	,,	10^{-7}	3·70	,,	,,	10^{-4}	22·1
,,	,,	10^{-6}	3·81	,,	,,	10^{-3}	20·8
,,	,,	10^{-5}	3·65				
,,	,,	10^{-4}	3·07	3	10	0	91
,,	,,	10^{-3}	2·03	,,	,,	10^{-4}	91·5
,,	2·5	0	9·74	,,	,,	10^{-3}	90
,,	,,	10^{-5}	9·70				
,,	,,	10^{-4}	8·49				
,,	,,	10^{-3}	7·05				

(Edwards, *Trans. Faraday Soc.*, 1952, **48**, 696). At pH 7·4, $k_{obs.} = 55{\cdot}5k_5 + k_s c_{OH}$ where, at 37°, $k_5 = 1{\cdot}64 \times 10^{-2}$ and $k_s = 1{\cdot}18 \times 10^5$, giving $k_{obs.} = 0{\cdot}92$.

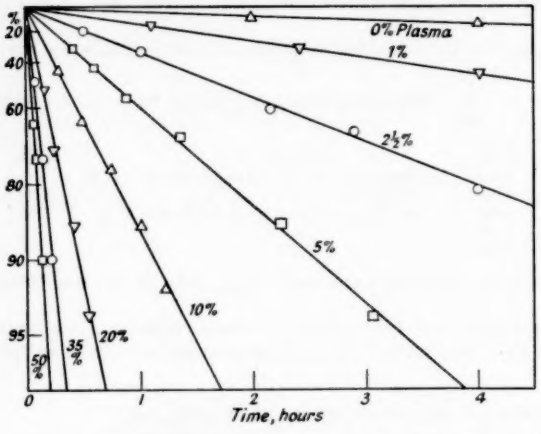

FIG. 1. *First-order rates of hydrolysis of aspirin at various plasma concentrations; plasma from guinea-pig no.* 2, 37°, *sodium citrate buffer* pH 7·4.

At substrate concentrations of 5×10^{-3} and above, the enzyme activity appeared to be at a maximum for plasma from guinea-pig no. 1. In subsequent experiments the substrate concentration was kept at this level. Esterase activity varied for different animals, as may be seen by comparing the $k_{obs.}$ values at the same plasma level.

In all cases the hydrolysis followed a first-order course and the experimental results for no. 2 plasma, illustrated in Fig. 1, are typical for the series.

When calcium aspirin was used in place of aspirin as substrate, the rate of the hydrolysis was much the same as before, although Ca^{++} is often a positive catalyst for esterase-catalysed reactions.

The enzyme activity was unaltered if the plasma was stored in the refrigerator for a week, but an hour's heating at 57° substantially destroyed the esterases and reduced the hydrolysis rate to the normal water-catalysed level (plasma no. 5).

The inhibitory action of physostigmine was examined at various concentrations. Although there was a certain amount of retardation of the hydrolysis at low plasma concentrations, yet comparatively massive doses of the inhibitor were required; at higher plasma concentrations amounts of physostigmine of up to 10^{-3}M had little effect on the reaction velocity.

DISCUSSION

By choosing the appropriate scale along the plasma-concentration axis the values for the esterase-catalysed reaction ($k_{obs.} - 0{\cdot}92$) could all be made to lie on a smooth curve (Fig. 2). In a system where

$$\text{enzyme} + \text{substrate} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{complex} \xrightarrow{k_3} \text{products}$$

the reaction rate is theoretically

$$-dc_s/dt = k_3 c_e c_s/(K + c_s)$$

K being the Michaelis constant $(k_2 + k_3)/k_1$. When the substrate concentration, c_s, is fixed, the rate should be proportional to the enzyme concentration, c_e. Fig. 2 shows that this relation is obeyed at plasma concentrations above *ca.* 10—15%. At the lower concentrations there is considerable departure from linearity. This is not unusual; Kraupp (*Z. Vitamin-, Hormon- u. Fermentforsch.*, 1949, **2**, 179) reported that large dilutions lower the activity of choline esterase, for example.

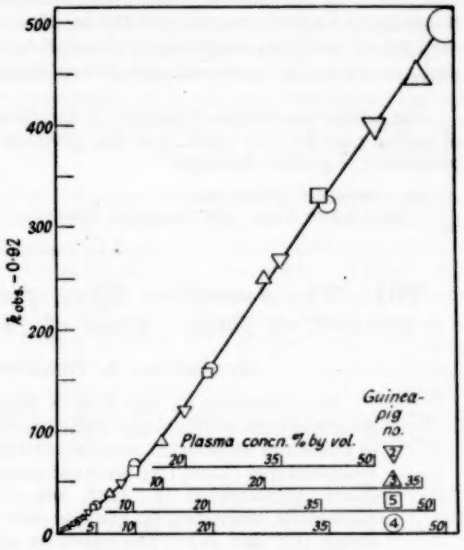

FIG. 2. *First-order velocity constants for the esterase-catalysed hydrolysis of aspirin as a function of plasma concentration : animals 2, 3, 5—substrate aspirin ; animal 4—substrate calcium aspirin.*

Some idea of the relative esterase concentrations in different individuals may be obtained by comparing the scale factors in Fig. 2. The mean value being taken as unity, the relative activities of the four plasma samples are :

Guinea-pig no.	2	3	4	5
Relative esterase activity	0·79	1·30	0·97	0·94

indicating that a deviation of at least 30% from the mean can be expected in different individuals.

If the linear portion of Fig. 2 is extrapolated to 100% plasma concentration, the corresponding reaction rates are :

Guinea-pig no.	2	3	4	5
$k_{obs.}$	860	1420	1060	1020
$t_{90\%}$ (min.)	3·8	2·3	3·1	3·2

It is noteworthy that to obtain a reaction velocity of this magnitude at 37° in the absence of catalysts other than those molecular and ionic species normally present in water it would be necessary to use a buffer solution of pH 12.

In applying these results to the hydrolysis *in vivo* of aspirin in the blood-stream some caution is needed. It must be borne in mind that (i) the whole blood of a living animal is being compared with the plasma from a dead animal; (ii) the plasma is citrated; (iii) the extrapolation from 50% to 100% plasma concentration assumes a linear relation which, although theoretically probable, has not been experimentally demonstrated. It seems likely, however, that the hydrolysis rate *in vivo* would not be less than that determined *in vitro*. If this argument is accepted it would follow that the life of aspirin in the blood-stream is quite short, 99% of the initial concentration being hydrolysed in about 5—10 minutes.

Lester, Lolli, and Greenberg (*J. Pharmacol.*, 1946, **87**, 329) recorded that aspirin is

rapidly hydrolysed on incubation at 37° with plasma. They gave no values for the reaction rate under these conditions but attempted to determine the aspirin concentrations in the plasma after oral administration by subtracting the free salicylate from the total salicylate (by hydrolysis of plasma). They found that 30 minutes after ingestion of 0·65 g. of aspirin 27% of the total blood salicylate was acetylsalicylate; at 120 minutes none could be detected. 70 Minutes after the ingestion of 2·60 g., 13% of the total was present as acetylsalicylate; at 160 minutes none could be detected. When allowance is made for the time taken for the aspirin to pass into the blood-stream and the possibility that their differential method of analysis might have overestimated the aspirin content of the blood, their findings are not inconsistent with the conclusions made from the present study.

The author thanks his colleagues in the Biological Department for maintaining the supply of guinea-pigs for this work, and the Directors of Beecham Research Laboratories Ltd. for permission to publish the paper.

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791. *The Associating Effect of the Hydrogen Atom. Part XV.* The* S–H–N *Bond. Esters of Thion- and Dithio-carbamic Acids.*

By ARNOLD A. BURROWS and LOUIS HUNTER.

New examples of the S–H–N bond are revealed by molecular-weight measurements of thion- and dithio-carbamic esters, which show a high degree of molecular association provided at least one amino-hydrogen atom remains unsubstituted (I and II); such compounds provide further examples of meso-hydric tautomerism (*J.*, 1945, 806). Association is destroyed, as well as tautomeric character, by the complete replacement of the amino-hydrogen atoms (III and IV). The effect on molecular association of certain *o*-substituents in phenyl-thion- and -dithio-carbamic esters is discussed in the light of steric and other effects.

IT has been pointed out in Part XI (*J.*, 1942, 638) that, although hydrogen bonds involving the sulphur atom are usually very weak, such bonds acquire considerable stability in compounds in which the hydrogen atom concerned has tautomeric character. Thus, although thioamides exhibit molecular association involving S–H–N bonds, thiols, thiophenols, and compounds containing cyclic sulphur atoms show no association.

This parallel between tautomeric character and molecular association due to S–H–N bonds has been further substantiated in the present investigation by the behaviour of the esters of thion- and dithio-carbamic acids. Provided these substances contain at least one unsubstituted (amino-)hydrogen atom (as in I and II) they are found to be markedly associated, but complete replacement of the amino-hydrogen atoms by alkyl, aryl, or acyl groups (as in III and IV) destroys their molecular association. Molecular association was assessed

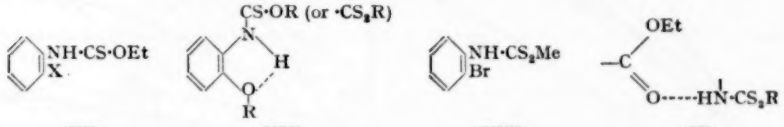
$NHR\cdot CS\cdot OR'$	$NHR\cdot CS_2R'$	$NR_2\cdot CS\cdot OR'$	$NR_2\cdot CS_2R'$	$NHR\cdot CO\cdot SEt$
(I)	(II)	(III)	(IV)	(V)

cryoscopically for benzene or naphthalene solutions and, as in previous Parts of this series, association is inferred from molecular-weight measurements in all cases in which the factor of association (α) increases substantially with rising concentration; *i.e.*, a steep association–concentration curve is taken to indicate molecular association, whereas a flat or gently sloped curve (in the region of $\alpha = 1$) is interpreted as indicating the absence of association. Association is assessed more from the slopes of these curves than from the absolute values of α, which may have no real significance and in many cases are less than unity. Figs. 1 and 2 provide numerous examples of these two sharply differentiated types, and it seems clear that esters such as (I) and (II) owe their molecular association no less than their tautomeric

* Part XIV, *J.*, 1950, 2857.

character to molecular union through S–H–N bonds, the amino-hydrogen atom of one molecule being shared with the (thion-)sulphur atom of an adjacent molecule. The type of polymer is therefore similar to that proposed for the esters of carbamic acid (Part XIII, *J.*, 1948, 874), and, since factors of association of similar magnitude are observed, it is reasonable to believe that the S–H–N bond in the compounds examined is as strong as the O–H–N bond in carbamic esters or in amides. This conclusion receives strong support from a comparison of the degrees of association of ethyl thioncarbamates (I ; R′ = Et) with the isomeric ethyl thiolcarbamates (V), owing their association respectively to S–H–N and O–H–N bonds. The slopes of the association–concentration curves (Fig. 3) of three pairs of such isomers show no significant differences; nor does the complete replacement of oxygen by sulphur in these compounds, as in the ethyl dithiocarbamates (II; R′ = Et), cause any considerable change of association, and it seems clear that provided such substances are of tautomeric type the resulting S–H–N bonds are as strong as those exhibited in their oxygen analogues.

A study has been made of the effect of substitution in the phenyl nucleus on the molecular association of phenyl-thion- and -dithio-carbamates. Fig. 3 shows that the high molecular association of ethyl phenylthioncarbamate (VI; X = H) is completely suppressed on substitution of a methoxyl-group in the *ortho*-position (VI; X = OMe). Indeed, the slope of the association–concentration curve of ethyl *o*-methoxyphenylthioncarbamate (VI; X = OMe) is comparable with that of its *N*-benzoyl derivative, which, owing to replacement of its amino-hydrogen atom, cannot possess a hydrogen-bond structure. On the other hand, substitution by methoxyl in the *para*-position, as in methyl and ethyl *p*-methoxyphenylthioncarbamates, does not significantly change the degree of association. Similar effects were observed in the methoxy- and ethoxy-phenyldithiocarbamates (Fig. 4), those having the substituent in the *ortho*-position (VI; X = OMe or OEt, S in place of O)



(VI) (VII) (VIII) (IX)

being markedly less associated than their *para*-isomers. The origin of this *ortho*-effect was at first supposed to be the tendency of the alkoxy-group to prevent a second molecule's approaching close enough to the amino-hydrogen atom to engage it in intermolecular S–H–N bond formation, thus substantially reducing the proportion of associated molecules. This mainly steric role, however, seems unlikely in view of the fact that other bulky groups, such as methyl and ethyl, when substituted *ortho* to the NH·CS·OR and NH·CS_2R groups, have no such effect. Thus, Figs. 1—3 provide many examples of *o*-tolyl- and *o*-ethylphenyl-substituted thion- and dithio-carbamic esters which possess association factors comparable with those of their *m*- and *p*-isomers. It therefore seems necessary to account for the absence of association in *o*-alkoxyphenyl-thion- and -dithio-carbamic esters by postulating the engagement of the amino-hydrogen atom in chelate-ring formation with the oxygen of the alkoxy-group (VII). The amino-hydrogen atom thus engaged is no longer available to link with the sulphur atom of a second molecule, and the structure thus favours the unimolecular state. The engagement of the oxygen atom of an alkoxy-group in chelate-ring formation with the hydrogen atom of an *ortho*-substituent has previously been suggested to account for the properties of guaiacol (Pauling, " Nature of the Chemical Bond," 2nd Edn., 1948, p. 324; Wulf and Deming, *J. Chem. Physics*, 1938, **6**, 702).

The reason for the reduced association of methyl *o*-bromophenyldithiocarbamate (VIII), compared with that of its *m*- and *p*- isomers (Fig. 5), is obscure. Without further investigation it is impossible to distinguish between a purely steric effect and a hydrogen bond (N–H–Br) similar to those suggested in ethylene bromohydrin, *o*-bromophenol, and tetrabromocatechol (Wulf, Liddel, and Hendricks, *J. Amer. Chem. Soc.*, 1936, **58**, 2287).

Factors other than steric effects must operate in the greatly increased slope of the

FIGS. 1—6.

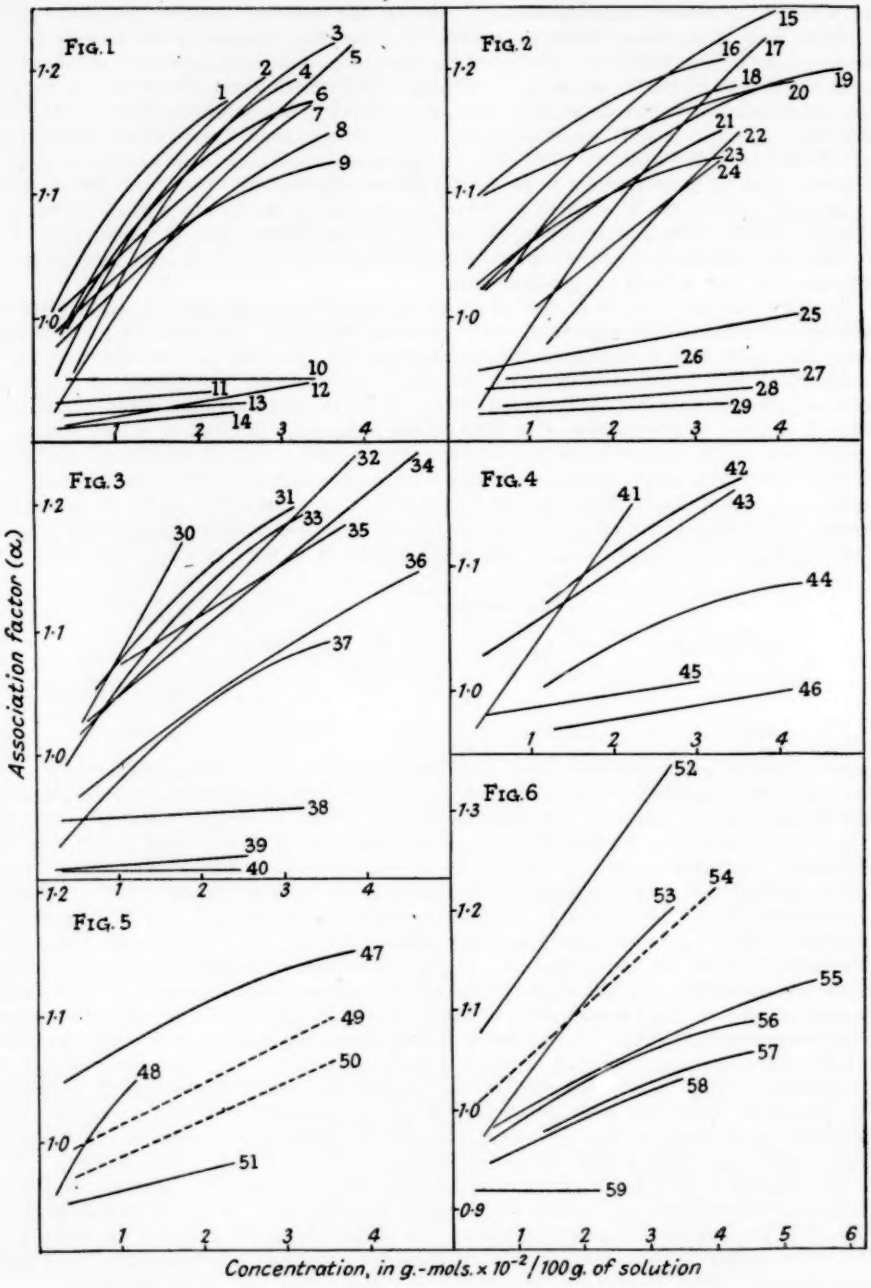


FIG. 1
FIG. 2
FIG. 3
FIG. 4
FIG. 5
FIG. 6
Association factor (α)
Concentration, in g.-mols. × 10⁻²/100 g. of solution

association–concentration curves of the *m*-carbethoxyphenyldithiocarbamates (Fig. 6), and it would appear that, in addition to S–H–N bonds due to association between NH·CS_2R groups, there may exist also heterogeneous association through N–H–O bonds between the carbethoxy-group of one molecule and the amino-hydrogen atom of another (as in IX). Effects of a similar kind have already been reported (Part XIII, *loc. cit.*, p. 877) between nitro- and amino-groups in nitrophenylcarbamates. On the other hand, the reduced association of methyl *cyclo*hexylthioncarbamate (Fig. 6) compared with that of methyl phenylthioncarbamate, is attributed to reduced acidity of the amino-hydrogen atom of the former owing to the absence of a mesomeric effect. Accountable in similar terms is the even more marked reduction in association revealed by comparing phenyl- with benzyl-thion- and -dithio-carbamates (Fig. 6). This dependence of association on the acidity of the hydrogen atom constituting the hydrogen bond has frequently been exemplified in previous Parts of this series.

Experimental

(Microanalyses were by Drs. Weiler and Strauss, Oxford.)

New *compounds* prepared during this investigation are given in the Table.

Thioncarbamic esters, R·NH·CS·OR′.

				Found, %				Required, %			
R′	R	Formula	M. p.	C	H	N	S	C	H	N	S
Me	*o*-Tolyl	$C_9H_{11}ONS$	76°	60·4	6·2	8·0	—	59·6	6·1	7·7	—
Me	*m*-Tolyl	$C_9H_{11}ONS$	43	60·0	6·2	8·0	—	59·6	6·1	7·7	—
Me	*p*-Tolyl	$C_9H_{11}ONS$	83	60·0	6·2	8·2	—	59·6	6·1	7·7	—
Et	*o*-MeO·C_6H_4	$C_{10}H_{13}O_2NS$	66	56·9	5·8	6·5	14·9	56·9	6·2	6·6	15·2
Me	*p*-MeO·C_6H_4	$C_9H_{11}O_2NS$	103	55·1	5·3	6·9	15·6	54·8	5·6	7·1	16·2
Et	*p*-MeO·C_6H_4	$C_{10}H_{13}O_2NS$	81	57·0	5·9	6·6	15·0	56·9	6·2	6·6	15·2
Me	CH_2Ph	$C_9H_{11}ONS$	49	—	—	—	18·1	—	—	—	17·7
Me	*cyclo*Hexyl	$C_8H_{15}ONS$	42	—	—	—	18·4	—	—	—	18·5

Fig. 1.

1, Ph·NH·CS·OBu^i
2, Ph·NH·CS·OBu^n
3, *p*-C_6H_4Me·NH·CS·OMe
4, Ph·NH·CS·OPr^i
5, Ph·NH·CS·OMe
6, *p*-C_6H_4Me·NH·CS·OEt
7, Ph·NH·CS·OPr^n
8, *m*-C_6H_4Me·NH·CS·OMe
9, *o*-C_6H_4Me·NH·CS·OMe
10, Ph·NBz·CS·OEt
11, *m*-C_6H_4Me·NBz·CS·OEt
12, *o*-C_6H_4Me·NBz·CS·OMe
13, Ph·NBz·CS·OMe
14, *p*-C_6H_4Me·NBz·CS·OEt

Fig. 3.

30, *p*-MeO·C_6H_4·NH·CS·OMe
31, Ph·NH·CS·OEt
32, *m*-C_6H_4Me·NH·CO·SEt
33, *p*-MeO·C_6H_4·NH·CS·OEt
34, Ph·NH·CO·SEt
35, *m*-C_6H_4Me·NH·CS·OEt
36, *o*-C_6H_4Me·NH·CO·SEt
37, *o*-C_6H_4Me·NH·CS·OEt
38, *o*-MeO·C_6H_4·NH·CS·OEt
39, *o*-MeO·C_6H_4·NBz·CS·OEt
40, *p*-MeO·C_6H_4·NBz·CS·OEt

Fig. 5.

47, *p*-C_6H_4Br·NH·CS_2Et
48, *p*-C_6H_4Br·NH·CS_2Me (in C_6H_6)
49, " (in $C_{10}H_8$)
50, *m*-C_6H_4Br·NH·CS_2Me (in $C_{10}H_8$)
51, *o*-C_6H_4Br·NH·CS_2Me

Fig. 2.

15, *o*-C_6H_4Et·NH·CS_2Me
16, 2 : 4 : 1-$C_6H_3Me_2$·NH·CS_2Me
17, Ph·NH·CS_2Me
18, *o*-C_6H_4Me·CS_2Et
19, 2 : 4 : 1-$C_6H_3Me_2$·NH·CS_2Et
20, *p*-C_6H_4Me·NH·CS_2Et
21, *m*-C_6H_4Me·NH·CS_2Me
22, *p*-C_6H_4Me·NH·CS_2Me
23, *m*-C_6H_4Me·NH·CS_2Et
24, Ph·NH·CS_2Et
25, *p*-C_6H_4Me·NMe·CS_2Et
26, Ph·NEt·CS_2Me
27, *p*-C_6H_4Me·NMe·CS_2Me
28, Ph·NMe·CS_2Et
29, Ph·NMe·CS_2Me

Fig. 4.

41, { *p*-MeO·C_6H_4·NH·CS_2Me / *p*-EtO·C_6H_4·NH·CS_2Me
42, *p*-MeO·C_6H_4·NH·CS_2Et
43, *p*-EtO·C_6H_4·NH·CS_2Et
44, *o*-MeO·C_6H_4·NH·CS_2Me
45, *o*-EtO·C_6H_4·NH·CS_2Et
46, *o*-EtO·C_6H_4·NH·CS_2Me

Fig. 6.

52, *m*-CO_2Et·C_6H_4·NH·CS_2Me
53, *m*-CO_2Et·C_6H_4·NH·CS_2Et
54, Ph·NH·CS·OMe (for comparison)
55, C_6H_{11}·NH·CS·OMe
56, CH_2Ph·NH·CS·OMe
57, CH_2Ph·NH·CS_2Me
58, CH_2Ph·NH·CS_2Et
59, CH_2Ph·NPh·CS_2Et

Thiolcarbamic ester, R·NH·CO·SR′.

R′	R	Formula	M. p.	Found, % C	H	N	S	Required, % C	H	N	S
Et	*m*-Tolyl	$C_{10}H_{13}ONS$	59	—	—	—	16·7	—	—	—	16·4

N-Benzoylthioncarbamic esters, R·NBz·CS·OR′.

Me	Ph	$C_{15}H_{13}O_2NS$	95	67·2	4·9	5·2	12·0	66·4	4·8	5·2	11·8
Et	Ph	$C_{16}H_{15}O_2NS$	84	67·8	5·2	4·8	11·1	67·3	5·3	4·9	11·2
Me	*o*-Tolyl	$C_{16}H_{15}O_2NS$	92	67·9	4·8	4·9	11·0	67·3	5·3	4·9	11·2
Et	*m*-Tolyl	$C_{17}H_{17}O_2NS$	96	67·0	5·8	4·6	10·0	68·2	5·7	4·7	10·7
Et	*p*-Tolyl	$C_{17}H_{17}O_2NS$	115	68·7	6·0	4·7	10·3	68·2	5·7	4·7	10·7
Et	*o*-MeO·C_6H_4	$C_{17}H_{17}O_3NS$	104	65·2	5·5	4·3	9·6	64·7	5·4	4·4	10·2
Et	*p*-MeO·C_6H_4	$C_{17}H_{17}O_3NS$	89	64·8	5·3	4·2	10·0	64·7	5·4	4·4	10·2

Dithiocarbamic esters, R·NH·CS_2R′.

Et	*m*-Tolyl	$C_{10}H_{13}NS_2$	63°	—	—	—	30·4	—	—	—	30·3
Me	*o*-C_6H_4Et	$C_{10}H_{13}NS_2$	75	—	—	—	30·8	—	—	—	30·3
Me	*p*-MeO·C_6H_4	$C_9H_{11}ONS_2$	101	—	—	—	29·5	—	—	—	30·1
Et	*p*-MeO·C_6H_4	$C_{10}H_{13}ONS_2$	77	—	—	—	28·6	—	—	—	28·2
Me	*o*-EtO·C_6H_4	$C_{10}H_{13}ONS_2$	52	—	—	—	28·2	—	—	—	28·2
Et	*o*-EtO·C_6H_4	$C_{11}H_{15}ONS_2$	79	—	—	—	27·1	—	—	—	26·6
Me	*p*-EtO·C_6H_4	$C_{10}H_{13}ONS_2$	104	—	—	—	28·1	—	—	—	28·2
Et	*p*-EtO·C_6H_4	$C_{11}H_{15}ONS_2$	93	—	—	—	26·7	—	—	—	26·6
Me	*m*-CO_2Et·C_6H_4	$C_{11}H_{13}O_2NS_2$	73	—	—	—	25·0	—	—	—	25·1
Et	*m*-CO_2Et·C_6H_4	$C_{12}H_{15}O_2NS_2$	67	—	—	—	23·2	—	—	—	23·8
Me	2 : 4 : 1-$C_6H_3Me_2$	$C_{10}H_{13}NS_2$	103	—	—	—	30·3	—	—	—	30·3
Et	2 : 4 : 1-$C_6H_3Me_2$	$C_{11}H_{15}NS_2$	65	—	—	—	28·4	—	—	—	28·4
Me	CH_2Ph	$C_9H_{11}NS_2$	57	—	—	—	32·9	—	—	—	32·5
Et	CH_2Ph	$C_{10}H_{13}NS_2$	52	—	—	—	29·8	—	—	—	30·3
				Br			S	Br			S
Me	*o*-C_6H_4Br	$C_8H_8NBrS_2$	100	31·0			24·4	30·5			24·5
Me	*m*-C_6H_4Br	$C_8H_8NBrS_2$	111	31·2			25·0	30·5			24·5
Me	*p*-C_6H_4Br	$C_8H_8NBrS_2$	120	31·1			24·3	30·5			24·5

Dithiocarbamic esters, RR′N·CS_2R″.

R″	R′	R	Formula	M. p.	Found, % C	H	N	S	Required, % C	H	N	S
Me	Me	*p*-Tolyl	$C_{10}H_{13}NS_2$	82°	—	—	—	29·6	—	—	—	30·3
Et	Me	*p*-Tolyl	$C_{11}H_{15}NS_2$	84	—	—	—	28·4	—	—	—	28·4
Et	CH_2Ph	Ph	$C_{16}H_{17}NS_2$	76	—	—	—	22·3	—	—	—	22·3

Revised m. p.s are recorded for the following: methyl phenylthioncarbamate, m. p. 98° (lit., 95—96, 97°), methyl *o*-tolyldithiocarbamate, m. p. 137° (lit., 132°), methyl *m*-tolyldithiocarbamate, m. p. 94° (lit., 89°), ethyl *N*-methyl-*N*-phenyldithiocarbamate, m. p. 99° (lit., 94·5—95·5°).

Molecular-weight Data.—Molecular weights were measured cryoscopically in benzene, with the two exceptions noted in Fig. 5, and were deduced according to ideal-solution laws. In the Figures concentrations are expressed as g.-mols. $\times 10^{-2}$/100 g. of solution, and the association factor (α) is calculated as the ratio of the apparent molecular weight to the formula weight.

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University College, Leicester. [*Received, May 24th*, 1951.]

792. *Adsorption from Binary Mixtures: Determination of Individual Adsorption Isotherms.*

By J. J. Kipling and D. A. Tester.

In adsorption on solid surfaces from binary liquid mixtures, the isotherms for adsorption of the individual components cannot be represented by simple Freundlich or Langmuir equations. An analysis based on the assumption that the surface is completely covered with adsorbate at all concentrations gives results in agreement with those obtained by direct adsorption from the corresponding vapour phase. A kinetic treatment is proposed for this type of adsorption. Vapour-pressure data required in this work are recorded for the systems benzene–ethyl alcohol and benzene–ethylene dichloride at 20°.

The development of theories of adsorption on to solid surfaces from binary liquid mixtures has been traced in a recent review (Kipling, *Quart. Reviews*, 1951, **5**, 60). What has conventionally been called the "adsorption isotherm" is now explained as the resultant of two individual isotherms (for the "solute" and "solvent" respectively) and is not itself a direct measure of the adsorption of either component. It could more accurately be described as the "isotherm of concentration change," as it is obtained directly from experimental measurement of this function. The term "selective adsorption" has also been proposed (Rao, *J. Phys. Chem.*, 1932, **36**, 616), but in the light of the present work, it seems unlikely to have precisely the significance originally intended.

The determination of the individual isotherms now becomes of great interest, but is not possible by any direct method. Two indirect methods have been proposed: (i) the testing of theoretical equations for the individual isotherms against experimental data on their resultants, (ii) investigation of adsorption through the vapour phase in equilibrium with the binary liquid mixture.

(1) *Bartell and Sloan's Method.*—The relation between the isotherm of concentration change and the individual adsorption isotherms has been given independently by Ostwald and de Izaguirre (*Kolloid-Z.*, 1922, **30**, 279) and Bartell and Sloan (*J. Amer. Chem. Soc.*, 1929, **51**, 1637, 1643), and can be written in the form: *

$$n_0(x_0 - x)/m = n_0\Delta x/m = n_1^s(1 - x) - n_2^s x \quad . \quad . \quad . \quad . \quad (1)$$

where, for a mixture of substances 1 and 2, x_0 is the mole-fraction of 1 in the mixture before, and x is that after adsorption; n_1^s and n_2^s are respectively the number of moles of 1 and of 2 adsorbed per g. of charcoal; m is the weight (g.) of charcoal used, and n_0 is the total number of moles in the original solution.

Bartell and Sloan assumed that the adsorption of each component followed a Freundlich equation. They thus obtained the following equation for the isotherm of concentration change:

$$n_0 \cdot \Delta x/m = k_1 \cdot x^\alpha(1 - x) - k_2(1 - x)^\beta \cdot x \quad . \quad . \quad . \quad . \quad (2)$$

By successive approximations they were able to deduce values of the four constants which made equation (2) fit their experimental results for a number of systems, and in particular the system benzene–ethyl alcohol with charcoal.

The Freundlich equation has been used empirically for adsorption from both the gaseous and the liquid phase. For the adsorption of gases it has been replaced (for unimolecular adsorption) by the more satisfactory Langmuir equation, which has kinetic, thermodynamic, and statistical derivations (Brunauer, "Physical Adsorption of Gases and Vapours," Oxford, 1944). We have therefore investigated the applicability of the

* As the symbols used in the literature have been very varied, an attempt has been made in this paper to establish a standard in accordance with the convention recently approved for this Journal (*J.*, 1951, 1677).

Langmuir equation to liquid systems, as it might be expected to prove more satisfactory than the Freundlich equation. In place of equation (2) it gives :

$$n_0 \cdot \Delta x/m = \frac{k_1'Kx(1-x)}{1+k_1'x} - \frac{k_2'K'x(1-x)}{1+k_2'(1-x)} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Repeating the adsorption from the system benzene–ethyl alcohol on a new sample of charcoal, we have found that the experimental data can be fitted as well by equation (3) as by equation (2), when the constants are : Freundlich, $k_1 = 11{\cdot}50$, $k_2 = 7{\cdot}72$, $\alpha = 0{\cdot}70$, $\beta = 0{\cdot}71$; Langmuir, $k_1' = 15{\cdot}6$, $k_2' = 50{\cdot}0$, $K = 3{\cdot}21$, $K' = 1{\cdot}00$, giving the curves

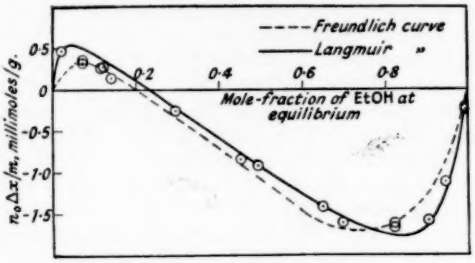


FIG. 1. *Isotherms of concentration change for the system benzene–ethyl alcohol.*

Points : experimental.
Curves : calculated.

shown in Fig. 1. This has already been briefly reported (Kipling and Tester, *Nature*, 1951, **167**, 612). The constants have been revised slightly from those published earlier. Those for the Freundlich method are very similar to those of Bartell and Sloan, although different charcoals were used.

In spite of the close agreement of these two treatments with each other and with the experimental data, a plot of the individual isotherms given by the two methods shows a

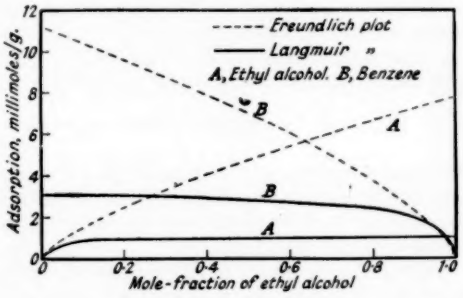


FIG. 2. *Individual adsorption isotherms for the system benzene–ethyl alcohol, plotted according to the Freundlich and the Langmuir equations.*

wide discrepancy (Fig. 2). This discrepancy clearly casts doubt on the validity of both of these treatments, which is further considered on p. 4128. Both treatments require saturation values for the separate components of the mixtures which do not agree with the experimental values of Table 1. In view of this, we have turned to the vapour phase in

TABLE 1. *Separate adsorption of ethyl alcohol and benzene at* 20°.

Benzene :		Ethyl alcohol :		Benzene :		Ethyl alcohol :	
p/p°	*w*, %	p/p°	*w*, %	p/p°	*w*, %	p/p°	*w*, %
0·051	22·2	0·030	13·9	0·344	25·6	0·401	22·4
0·076	23·2	0·117	19·4	0·423	26·2	0·607	23·7
0·108	24·3	0·152	20·4	0·656	26·2	0·683	23·7
0·193	23·8	0·208	20·9			0·803	23·9

the hope of obtaining reliable individual isotherms, and have then proposed two methods for describing the results.

(2) *Adsorption from the Vapour Phase.*—In adsorption from the vapour phase, measurements can be made both of the total weight of material adsorbed by the solid (which is not possible in adsorption from solutions), and of the change thus caused in the concentration of the liquid producing the vapour. It is then possible to determine the two individual adsorption isotherms directly. Provided that the mode of adsorption from the two phases is the same, then these must also be the individual isotherms for adsorption directly from

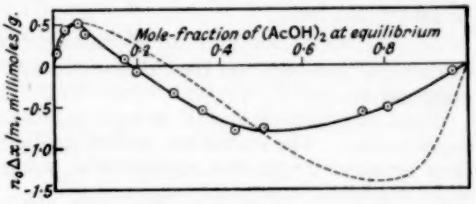


FIG. 3. *Isotherm of concentration change for adsorption from benzene–acetic acid mixtures.*

Points : experimental.
Broken curve : calculated.

the liquid phase. Agreement has previously been found between isotherms of concentration change for adsorption from the vapour and liquid phases (Innes and Rowley, *J. Phys. Coll. Chem.*, 1947, **51**, 1172), but not for the individual isotherms.

Measurements of adsorption from the vapour phase are shown in Figs. 5, 6, and 7 for three systems. The corresponding isotherms of concentration change (obtained from the

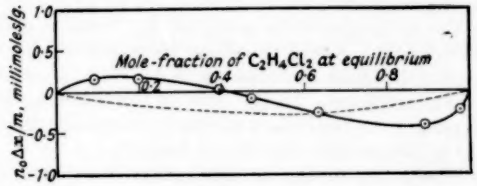


FIG. 4. *Isotherm of concentration change for adsorption from benzene–ethylene dichloride mixtures.*

Points : experimental.
Broken curve : calculated.

liquid phase) are given in Figs. 1, 3, and 4. In the system benzene–acetic acid, it is assumed that the acetic acid is present as the dimeric molecule over effectively the whole of the concentration range, and that it is adsorbed in that form.

It will be seen that the individual isotherms for the benzene–ethyl alcohol system (Fig. 5) bear little resemblance to either set shown in Fig. 2. It follows that equations

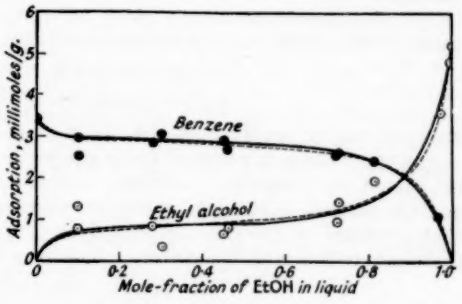


FIG. 5. *Adsorption from benzene–ethyl alcohol vapour mixtures : individual isotherms.*

Points : experimental.
Full curves : calculated (Section 3).
Broken curves : calculated (Section 4).

different from the simple Freundlich or Langmuir equations are required to describe them. To this end, we suggest two theoretical treatments, one based on a consideration of the nature of the adsorbed phase, the second a possible kinetic mechanism by which adsorption equilibrium is reached.

(3) *Nature of the Adsorbed Phase.*—Elton (*J.*, 1951, 2958) has recently pointed out an essential difference between adsorption from the liquid phase and most cases of adsorption from the gaseous phase, *viz.*, that the surface of the adsorbent is completely covered by liquid at all concentrations. We have, independently, reached the same conclusion, and

have based on it an analysis of the isotherms of concentration change. For unimolecular adsorption, it can be expressed in the form (cf. Elton, *loc. cit.*) :

$$n_1^s \cdot A_1 + n_2^s \cdot A_2 = A \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where A_1 and A_2 are the areas occupied by 1 mole of components 1 and 2, respectively, when adsorbed in a monolayer, and A is the total surface area of 1 g. of adsorbent : A_1 and A_2 can be obtained from published or calculated results. Alternatively, equation (4) can be used in the form :

$$n_1^s/(n_1^s)^\circ + n_2^s/(n_2^s)^\circ = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where $(n_1^s)^\circ$ and $(n_2^s)^\circ$ are the values obtained for adsorption from the vapours of the pure components.

From equations (5) and (1) we have calculated values of n_1^s and n_2^s for the three systems under review. The results are plotted in Figs. 5, 6, and 7. It will be seen that there is close agreement with the experimental points obtained from vapour-phase adsorption, which the earlier treatments have not given.

Table 1 gives the data for the isotherms of benzene and ethyl alcohol when adsorbed separately from the vapour phase on the charcoal used in these experiments. These values are in accordance with Langmuir's equation for unimolecular adsorption, giving values of 3·44 and 5·34 mmoles/g. of benzene and ethyl alcohol respectively for complete covering of the surface, though experimentally some capillary condensation is found at saturation. The corresponding value for carbon tetrachloride is 3·12 mmoles/g. Assuming that this has a spherical molecule occupying an area (calculated from the equation given by Brunauer, *op. cit.*, p. 287) of 30·6 sq. Å, we find that the molecular areas occupied by benzene and ethyl alcohol respectively are 27·8 and 17·9 sq. Å. These are close to the theoretical values of 27·1 sq. Å for edge-wise adsorption of benzene and 18·4 sq. Å for ethyl alcohol oriented with its major axis perpendicular to the surface. In the light of this evidence it seems not unreasonable to assume that adsorption from the binary mixtures is unimolecular and that equations (4) and (5) are therefore appropriate in the above analysis.

(4) *Suggested Kinetic Treatment.*—Any kinetic treatment of adsorption from binary liquid mixtures must be capable of adaptation to adsorption from the corresponding vapours, and *vice versa*. We suggest now a possible treatment for adsorption from binary vapour mixtures, and show how it can be adapted to apply to adsorption from liquids, and how it can be derived directly for adsorption from liquids. It is based on the assumption that, under all conditions of equilibrium, the surface is completely covered with a unimolecular layer of adsorbate.

(a) *Application to vapour-phase adsorption.* Let σ_1 and σ_2 be the fractions of the surface respectively covered by the two components. Then :

$$\text{rate of desorption of vapour}_1 = k_0\sigma_1 e^{-Q_1/RT}$$
$$\text{rate of desorption of vapour}_2 = k_0'\sigma_2 e^{-Q_2/RT}$$

where Q_1 and Q_2 are the respective heats of desorption.

As the surface is assumed to be completely covered, the rate of adsorption cannot be calculated by Langmuir's original method (*J. Amer. Chem. Soc.*, 1918, **40**, 1361). We assume, instead, that when adsorption sites become available (by the desorption process), they are filled by the two components in proportion to the rates at which their respective molecules collide with the surface. The rates of collision with a surface of area A are :

$$\text{for vapour}_1, \text{ rate} = ANp_1(1/2\pi M_1 RT)^{\frac{1}{2}}$$
$$\text{for vapour}_2, \text{ rate} = ANp_2(1/2\pi M_2 RT)^{\frac{1}{2}}$$

For kinetic equilibrium, the ratio of the rates of adsorption must equal the ratio of the rates of desorption, whence :

$$\sigma_1 k_0 e^{-Q_1/RT}/(1 - \sigma_1)k_0' e^{-Q_2/RT} = (p_1/M_1^{\frac{1}{2}})/(p_2/M_2^{\frac{1}{2}})$$

Therefore

$$\sigma_1 = p_1/[p_1 + p_2 k_0 M_1^{\frac{1}{2}} e^{(Q_2 - Q_1)/RT}/k_0' M_2^{\frac{1}{2}}]$$
$$= p_1/(p_1 + Kp_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$
$$= x^v/[x^v + K(1 - x^v)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where x^v is the mole-fraction of vapour$_1$ in the vapour phase. Similarly

$$\sigma_2 = Kp_2/(p_1 + Kp_2) = p_2/(p_2 + p_1/K)$$

Two methods are available for the determination of K. For σ_1 we can write $m_1/(m_1)^\circ$, where m_1 and $(m_1)^\circ$ g. are the weights of vapour$_1$ adsorbed per g. of adsorbent from a given mixture and from the pure component, respectively. Then

$$[(m_1)^\circ/m_1 - 1]p_1/p_2 = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Alternatively, K can be obtained from the isotherms of the separate components when adsorbed alone on the same solid. If the equations for these adsorption isotherms are written in the form $m/m^\circ = p/(1 + \beta p)$, then from the derivation of the Langmuir equation, we have

$$\beta_1 = N/[(2\pi M_1 RT)^{\frac{1}{2}} k_0 e^{-Q_1/RT}]$$
$$\beta_2 = N/[(2\pi M_2 RT)^{\frac{1}{2}} k_0' e^{-Q_2/RT}]$$

and
$$K(= k_0 M_1^{\frac{1}{2}} e^{-Q_1/RT}/k_0' M_2^{\frac{1}{2}} e^{-Q_2/RT}) = \beta_2/\beta_1$$

(b) *Adaptation to liquid-phase adsorption.* Equation (6) can be modified for use in liquid-phase adsorption by relating p_1 to x. Two important cases arise.

Case 1. In the ideal case, in which Raoult's law is obeyed, *i.e.*, $p_1 = p_1^\circ x$, equation (6) becomes

$$\sigma_1 = p_1^\circ x/[p_1^\circ x + Kp_2^\circ(1 - x)]$$

or
$$\sigma_1 = x/[x + K'(1 - x)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The equation for the isotherm of concentration change now becomes:

$$\frac{n_0 \Delta x}{m} = \frac{Ax(1 - x)/A_1}{x + K'(1 - x)} - \frac{AK'x(1 - x)/A_2}{x + K'(1 - x)}$$
$$= \frac{x(1 - x)A\left[\frac{1}{A_1} - \frac{K'}{A_2}\right]}{x + K'(1 - x)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The form of this equation should be noted. It gives zero apparent adsorption only when $x = 0$, $x = 1$, or when $1/A_1 = K'A_2$. It follows that, unless this last condition is fortuitously obeyed, the isotherm of concentration change must have the form of the calculated curve in Fig. 4, *i.e.*, the adsorption of one component will appear positive and that of the other component negative at all concentrations.

Case 2. For most systems, Raoult's law is not obeyed, and a different relationship between p_1 and x is required. Margules's equation (*Sitzungsber. Akad. Wiss. Wien*, 1895, **104**, 1243) may then be appropriate. The form of this equation which has been used in vapour studies of most such systems contains two terms in the exponential factor. This form is likely to have the most general application to adsorption studies. The alternative forms of the equation, with one, or with three or more terms, could, of course, be used where appropriate, as could any other equation having the same effect. The equation

$$p_1 = p_1^\circ x e^{\frac{1}{2}\alpha_3(1 - x)^2 + \frac{1}{3}\alpha_3(1 - x)^3}$$

leads to
$$\sigma_1 = x/\{x + K'(1 - x)e^{[-\frac{1}{2}\alpha_3 x^2 + (\alpha_3 + \alpha_2)x - \frac{1}{2}\alpha_3 - \frac{1}{3}\alpha_3]}\} \quad . \quad . \quad . \quad . \quad (11)$$

and hence
$$n_0 \Delta x/m = \frac{x(1 - x)A\left\{\frac{1}{A_1} - \frac{K'e^{[-\frac{1}{2}\alpha_3 x^2 + (\alpha_3 + \alpha_2)x - \frac{1}{2}\alpha_3 - \frac{1}{3}\alpha_3]}}{A_2}\right\}}{\{x + K'(1 - x)e^{[-\frac{1}{2}\alpha_3 x^2 + (\alpha_3 + \alpha_2)x - \frac{1}{2}\alpha_3 - \frac{1}{3}\alpha_3]}\}} \quad . \quad . \quad . \quad (12)$$

This equation can give the sigmoid form usually observed, the curve cutting the concentration axis when

$$1/A_1 = K'e^{[-\frac{1}{2}\alpha_3 x^2 + (\alpha_3 + \alpha_2)x - \frac{1}{2}\alpha_3 - \frac{1}{3}\alpha_3]}/A_2,$$

i.e., when

$$x = \left[(\alpha_3 + \alpha_2) \pm \sqrt{\alpha_3^2 + 2\alpha_2\alpha_3 + \alpha_2^2 - 2\alpha_3\left(\frac{\alpha_2}{2} + \frac{\alpha_3}{3} + \ln\frac{A_2}{A_1K_1}\right)}\right]\Big/\alpha_3$$

provided that this gives one positive root. The constants may be such that there is no real root between 0 and 1, in which case a sigmoid curve will not be obtained. Curves have been published in which there is no negative branch, even though the system in question does not obey Raoult's law, *e.g.*, for the system methyl alcohol–benzene with silica gel (Bartell and Scheffler, *J. Amer. Chem. Soc.*, 1931, **53**, 2507).

(c) *Direct application to the liquid-phase adsorption.* An equation having the same form as (6) can be derived directly by applying the same kinetic treatment to the liquid phase. Then

$$\sigma_1 k_0 e^{-Q_3/RT}/(1-\sigma_1)k_0' e^{-Q_4/RT} = (a_1 M_1^{\frac{1}{2}})/(a_2/M_2^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad (13)$$

where a_1 and a_2 are the activities of the first and the second component, respectively, in the liquid phase, and Q_3 and Q_4 the respective heats of desorption into the liquid phase. Then

$$\sigma_1 = a_1/(a_1 + K''a_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where

$$K'' = (k_0 M_1^{\frac{1}{2}}/k_0' M_2^{\frac{1}{2}}) e^{(Q_4 - Q_3)/RT}$$

This is of the same form as equation (6) for adsorption from the vapour phase. K and K'' are not equal, but can be related as follows. Let L_1 and L_2 be the molar heats of vaporisation of the two components. Then

$$Q_4 - Q_3 = (Q_2 - L_2) - (Q_1 - L_1)$$

From the Clapeyron–Clausius equation,

$$\mathrm{d} \ln p_1^\circ/\mathrm{d}T = L_1/RT^2 \text{ and } \mathrm{d} \ln p_2^\circ/\mathrm{d}T = L_2/RT^2$$

whence $\ln p_1^\circ = -L_1/RT + c_1$, and $\ln p_2^\circ = -L_2/RT + c_2$, on the assumption that L_1 and L_2 vary only slightly with temperature, c_1 and c_2 being constants. Then

$$p_1^\circ/c_1' = e^{-L_1/RT} \text{ and } p_2^\circ/c_2' = e^{-L_2/RT}$$

where $\ln c_1' = c_1$, and $\ln c_2' = c_2$.

Hence

$$c_2' p_1^\circ/c_1' p_2^\circ = e^{(L_2 - L_1)/RT}$$

and

$$K'' = (k_0 M_1^{\frac{1}{2}} p_2^\circ c_1'/k_0' M_2^{\frac{1}{2}} p_1^\circ c_2') e^{(Q_4 - Q_3)/RT} = K p_2^\circ c_1'/p_1^\circ c_2'$$

For most simple pairs of organic liquids, $c_1'/c_2' = 1$ as a first approximation, so that $K'' \sim p_2^\circ K/p_1^\circ = K'$. As $a_1 = p_1/p_1^\circ$, equation (14) becomes identical with equation (9) if Raoult's law is obeyed, and with equation (11) if Margules's equation is appropriate.

Discussion

Nature of the Adsorbed Phase.—As the treatment proposed in Section (3) seems to offer a satisfactory interpretation of the experimental data, it may be relevant to examine the deficiencies of those used in Section (1). The argument is based on the assumption that the adsorbing surface is completely covered at all liquid concentrations. If the Langmuir equations are used in the form

$$n_1^s = \frac{k_1 K_1 x}{1 + k_1 x}, \quad n_2^s = \frac{k_2 K_2 (1-x)}{1 + k_2(1-x)} \quad . \quad . \quad . \quad . \quad . \quad (15)$$

then equation (4) becomes

$$\frac{A_1 k_1 K_1 x}{1 + k_1 x} + \frac{A_2 k_2 K_2 (1-x)}{1 + k_2(1-x)} = A$$

This is a quadratic equation in terms of x, and hence can, in general, only have two solutions for x. The experimental data, however, require an equation which will give a number of solutions for x which approaches infinity. It therefore follows that the Langmuir equation cannot be used in this form in the present theory of adsorption. A similar difficulty confronts the use of the Freundlich equation. This conclusion had been foreshadowed (Kipling and Tester, *loc. cit.*).

Kinetic Treatment.—The suggested kinetic treatment shows some similarity to that of Tryhorn and Wyatt (*Trans. Faraday Soc.*, 1928, **24**, 36) which appears, implicitly, also to

have been based on the assumption that the adsorbing surface is at all times completely covered. This treatment, however, neglected any consideration of the desorption process and did not therefore give a picture of kinetic equilibrium as usually understood.

Equation (6) is also similar to that of Markham and Benton (*J. Amer. Chem. Soc.*, 1931, **53**, 497; cf. also Kemball, Rideal, and Guggenheim, *Trans. Faraday Soc.*, 1948, **44**, 948), which is, however, normally used for cases in which the surface is only fractionally covered. The present treatment is put forward to emphasise the specific conditions applying to saturated vapours, but can be regarded as the limiting case of Markham and Benton's treatment when the free surface tends to zero. In the form of equation (6) it can more usefully be applied to deriving an equation for the isotherm of concentration change.

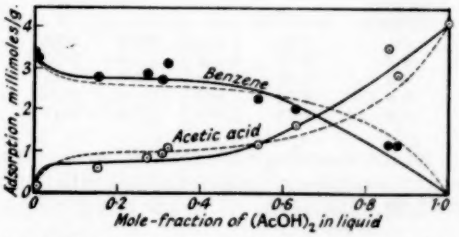


FIG. 6. *Adsorption from benzene–acetic acid vapour mixtures: individual isotherms.*

Points: experimental.
Full curves: calculated (Section 3).
Broken curves: calculated (Section 4).

A preliminary investigation of the usefulness of equation (6), and those which follow from it, has been made by reference to data on the three systems already discussed. Calculations of K have been made and are presented in Tables 2, 3, and 4. There is considerable variation in all three cases, from which we deduce that the activity coefficients for the adsorbed substances depart considerably from unity. This is not entirely unexpected when such factors as molecular interaction and difference in packing of the two components in relation to adsorption sites are considered.

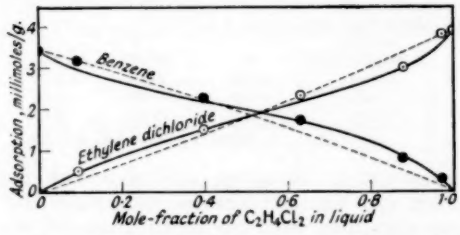


FIG. 7. *Adsorption from benzene–ethylene dichloride mixtures. True adsorption isotherms.*

Points: adsorption from vapour.
Full curves: calculated (Section 4).
Broken curves: calculated (Section 5).

In spite of this limitation, we have used mean values of K in further calculations, in order to draw a number of qualitative conclusions. First, the individual adsorption isotherms have been calculated, as a function of liquid-phase concentration, for the three systems, equations (9) and (11) being used. The resulting curves are shown in Figs. 5, 6, and 7. They are of substantially the same form as those obtained experimentally, which suggests that the activity–concentration relationship for the liquid mixtures plays a major part in determining the shape of the individual adsorption isotherms. A less precise form of this conclusion was suggested earlier by Tryhorn and Wyatt (*loc. cit.*).

TABLE 2. *Adsorption of ethyl alcohol vapour from mixtures with benzene.*

Mole-fraction of EtOH in liquid	$(m_1)^\circ/m_1$	p_1	p_2	K	Mole-fraction of EtOH in liquid	$(m_1)^\circ/m_1$	p_1	p_2	K
0·05	10·4	18·4	73·4	2·66	0·5	6·04	32·5	65·0	2·51
0·1	7·54	22·4	72·5	2·02	0·6	5·00	33·8	61·0	2·22
0·2	6·75	25·6	71·0	2·08	0·7	3·91	35·0	54·0	1·89
0·3	6·57	28·3	69·5	2·27	0·8	2·87	37·5	42·5	1·65
0·4	6·50	30·5	67·5	2·49	0·9	2·08	41·0	27·2	1·63

Mean value of K = 2·1

TABLE 3. *Adsorption of ethylene dichloride vapour from mixtures with benzene.*

Mole-fraction of $C_2H_4Cl_2$ in liquid	$(m_1)^\circ/m_1$	p_1	p_2	K	Mole-fraction of $C_2H_4Cl_2$ in liquid	$(m_1)^\circ/m_1$	p_1	p_2	K
0·1	7·37	6·2	66·75	0·59	0·6	1·80	36·7	29·5	1·00
0·2	4·83	12·25	59·25	0·79	0·7	1·59	43·0	22·1	1·15
0·3	3·13	18·5	52·0	0·76	0·8	1·42	49·0	15·0	1·37
0·4	2·49	24·5	44·5	0·82	0·9	1·245	55·0	7·5	1·80
0·5	2·09	30·6	37·0	0·90			Mean value of K = 1·0		

TABLE 4. *Adsorption of acetic acid vapour from mixtures with benzene.*

Mole-fraction of AcOH (dimer) in liquid	$(m_1)^\circ/m_1$	p_1	p_2	K	Mole-fraction of AcOH (dimer) in liquid	$(m_1)^\circ/m_1$	p_1	p_2	K
0·1	7·23	8·0	67·0	0·74	0·6	2·85	9·5	45·0	0·39
0·2	5·28	8·5	65·6	0·55	0·7	2·01	10·0	35·0	0·29
0·3	4·58	9·0	63·0	0·51	0·8	1·53	10·9	24·0	0·24
0·4	3·93	9·0	59·0	0·45	0·9	1·23	12·0	13·0	0·21
0·5	3·75	9·2	53·0	0·48			Mean value of K = 0·43		

Of the several systems recorded in the literature, we have chosen as an example that of methyl alcohol–carbon tetrachloride with charcoal (Innes and Rowley, *J. Phys. Coll. Chem.*, **1947**, **51**, 1154, 1172). The data here require a modification of equation (7) to the form

$$x_1^s = x^v/[x^v + kK(1 - x^v)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

where x_1^s is the mole-fraction of component 1 in the adsorbed phase. Then

$$x^v/x_1^s = kK + (1 - kK)x^v$$

where k is the ratio $(n_2^s)^\circ/(n_1^s)^\circ$ of the number of moles of the two components required to cover 1 g. of the surface completely. Table 5 shows the derivation of the value of kK,

TABLE 5. *Adsorption of carbon tetrachloride vapour from mixtures with methyl alcohol.*

Mole-fraction of CCl_4 in vapour (x^v)	x^s	x^v/x^s	kK	Mole-fraction of CCl_4 in vapour (x^v)	x^s	x^v/x^s	kK
0·11	0·115	0·96	0·96	0·43	0·49	0·88	0·79
0·12	0·185	0·65	0·60	0·49	0·56	0·88	0·76
0·16	0·20	0·80	0·76	0·58	0·62	0·94	0·86
0·23	0·29	0·79	0·73			Mean value of kK = 0·78	

from which the curve in Fig. 8 has been calculated. It agrees very well with the experimental data and is also in close agreement with Fig. 3 of Elton's recent paper (*loc. cit.*), which gives the corresponding curve for adsorption from the liquid phase for the same system.

For comparison, Fig. 9(*b*) gives our results for the ethyl alcohol–benzene system, also plotted in terms of x_1^s. Fig. 9(*a*) shows the fraction of the surface covered by each component as a function of vapour composition.

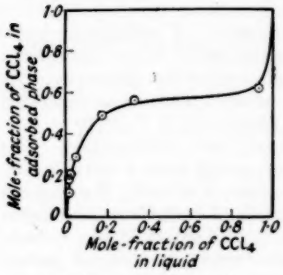
We have also examined the use of equations (10) and (12) for constructing the isotherm of concentration change. The result for the benzene–ethyl alcohol system (Fig. 10) is slightly better than those derived on the earlier basis (Fig. 1). The values of α_2 and α_3, the Margules constants, have been derived from vapour-pressure data given on p. 4132.

The benzene–ethylene dichloride system obeys Raoult's law very closely, and thus the calculated curve shows only one branch. The experimental curve, however, shows two branches, though these rise to only very small values, as will be seen from a comparison of Figs. 4 and 1, which are plotted on the same scale. We conclude that the behaviour of the system in the adsorbed phase is not ideal. As it has been suggested that the behaviour of this system in the liquid phase is only pseudo-ideal, it is hoped later to investigate systems in which more nearly ideal behaviour might be expected in both the liquid and the adsorbed phase.

The benzene–acetic acid system was chosen in order to investigate the effect of

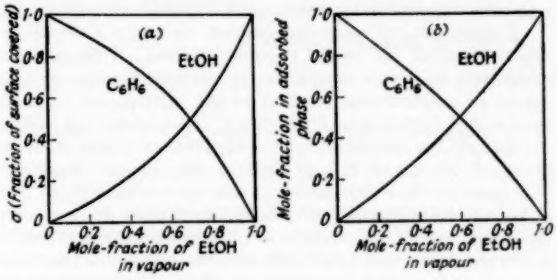
dimerisation of one component. We are satisfied that the acetic acid is essentially dimeric throughout, and that the presence of monomer can be neglected, except in very dilute solutions. The calculated isotherm of concentration change (Fig. 3) departs considerably from the experimental points in concentrated acetic acid solutions, more acetic acid being adsorbed than predicted theoretically. It is possible that the "excess" is adsorbed chemically by the small amount of alkaline ash in the charcoal, the presence of which has been demonstrated.

FIG. 8. *Adsorption from carbon tetrachloride–methyl alcohol vapour mixtures.*



Points : experimental.
Curve : calculated.

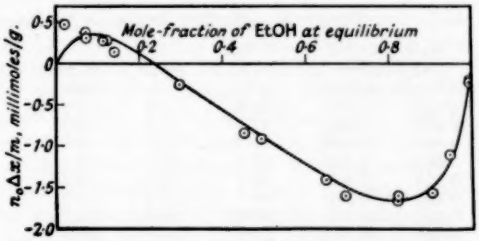
FIG. 9. *Adsorption from benzene–ethyl alcohol vapour mixtures.*



Finally, it may be noticed that equations (10) and (12) assume approximately the form of a Langmuir equation for dilute solutions, when both $(1 - x)$ and the exponential term approach 1. This explains the success which has been found in the past in applying Langmuir- or Freundlich-type equations to isotherms of concentration change. Such work has usually been done on dilute solutions, with a very small range of mole-fractions. This has been particularly the case with aqueous solutions, in which the small molecular weight of water makes a solution much more dilute in terms of mole fraction than it appears

FIG. 10. *Isotherm of concentration change for adsorption from benzene–ethyl alcohol mixtures.*

Points : experimental.
Curves : calculated.



when considered in terms of weight fraction or normality. Even for dilute solutions, it should be emphasised that the equations have not the same significance as has the true Langmuir equation for gaseous adsorption. Thus the constants do not give immediately a value for the surface area of the adsorbent in the way that is familiar for gaseous adsorption. Attention has already been drawn, in general terms, to the inadequacies of apparent adsorption data for determinations of surface areas (Kipling, *loc. cit.*).

EXPERIMENTAL

Materials.—The adsorbent was a commercial steam-activated coconut-shell charcoal, used in B.S.S. grading 20—40. Before use it was dried at 120°.

Benzene was dried over phosphoric oxide and fractionally distilled. Further impurities were removed by fractional crystallisation, until the whole yield froze at 5·5°. The purified benzene had d_4^{20} 0·8788, n_D^{20} 1·5010, in agreement with values quoted by Timmermans ("Physico-Chemical Constants of Pure Organic Compounds," London, 1950).

Ethyl alcohol was dried over calcium oxide. Remaining traces of water were removed by refluxing the alcohol with sodium wire and ethyl phthalate. The alcohol was then distilled; it had b. p. 78·2°, d_4^{20} 0·7895, n_D^{20} 1·3617.

Ethylene dichloride was fractionally distilled, the fraction used having n_D^{20} 1·4449, in good agreement with Coulson, Hales, and Herington's value (*Trans. Faraday Soc.*, 1948, **44**, 636).

Acetic acid, purified by Orton and Bradfield's method (*J.*, 1927, 983), had m. p. 16·6°, n_D^{20} 1·3718.

Procedure.—The determinations were all carried out in a 20° thermostat. For the liquid-phase experiments, sealed tubes containing charcoal and the mixtures were shaken in the thermostat for not less than 12 hours. For vapour-phase experiments, charcoal, in a small container, was suspended in the vapour above the appropriate liquid mixture, contained in a sealed vessel, and was weighed at intervals until equilibrium was attained.

Concentrations were determined by using a Pulfrich refractometer. A calibration curve was prepared for each system studied. Differences in concentration were determined accurately by direct comparison of the solutions before and after adsorption had taken place, by means of a differential reading on the instrument. The detailed procedure has been described earlier, *e.g.*, by Kane and Jatkar (*J. Indian Inst. Sci.*, 1938, **21**, *A*, 331).

Adsorption isotherms for the separate components were determined by a flow method. The charcoal, contained in a perforated aluminium " bucket," was suspended from a spiral spring in a chamber in a thermostat. Adsorption took place from air streams containing the vapours at known partial pressures. A stream of pure, dry air was passed through a saturator containing the liquid under investigation. It was then mixed with a second air stream in proportions determined by calibrated flow-meters, to give a combined stream having the desired partial pressure of the substance to be adsorbed. The weight of the adsorbate was calculated from the extension of the spiral spring, which was read by means of a cathetometer.

Partial Pressures.—Partial presssures at 20° were required for each of the systems studied. Tryhorn and Wyatt (*Trans. Faraday Soc.*, 1926, **21**, 399) recorded the composition of the vapour phase in the benzene–ethyl alcohol system as a function of that of the liquid phase, but did not give the total pressures from which the partial pressures could be deduced. These were therefore determined by Rosanoff's method (*J. Amer. Chem. Soc.*, 1914, **36**, 1803), by using a simplified form of the apparatus described by Hovorka and Dreisbach (*ibid.*, 1934, **56**, 1664). The results are given in Table 6. When expressed in terms of mole-fractions, they agree closely with Tryhorn and Wyatt's data.

TABLE 6. *Partial pressures for benzene–ethyl alcohol mixtures at* 20°.

Mole-fraction of EtOH: in liquid	in vapour	Total v. p. (mm.)	p_{EtOH} (mm.)	$p_{C_6H_6}$ (mm.)	Mole-fraction of EtOH: in liquid	in vapour	Total v. p. (mm.)	p_{EtOH} (mm.)	$p_{C_6H_6}$ (mm.)
0·000	0·000	74·3	0·0	74·3	0·4975	0·330	97·8	32·3	65·5
0·015	0·064	78·0	5·0	73·0	0·525	0·340	96·7	32·9	63·8
0·0275	0·058	85·7	12·7	73·0	0·640	0·368	92·7	34·1	58·6
0·065	0·216	93·6	20·2	73·4	0·724	0·604	87·6	35·4	52·2
0·210	0·269	96·2	25·9	70·3	0·806	0·490	80·0	39·2	40·8
0·231	0·272	97·5	26·4	71·0	0·935	0·686	62·8	43·1	19·7
0·320	0·295	97·5	28·8	68·7	1·000	1·000	44·7	44·7	0·0
0·335	0·2975	97·4	29·0	68·4					

TABLE 7. *Partial pressures for benzene–ethylene dichloride mixtures at* 20°.

Mole-fraction of $C_2H_4Cl_2$: in liquid	in vapour	Total v. p. (mm.)	$p_{C_2H_4Cl_2}$ (mm.)	$p_{C_6H_6}$ (mm.)	Mole-fraction of $C_2H_4Cl_2$: in liquid	in vapour	Total v. p. (mm.)	$p_{C_2H_4Cl_2}$ (mm.)	$p_{C_6H_6}$ (mm.)
0·000	0·000	74·3	0·0	74·3	0·6325	0·595	65·5	39·0	26·5
0·040	0·0325	73·8	2·4	71·4	0·680	0·635	65·0	41·3	23·7
0·0465	0·041	73·6	3·0	70·6	0·773	0·741	64·5	47·8	16·7
0·2875	0·254	70·5	17·9	52·6	0·793	0·756	64·1	48·5	15·6
0·344	0·305	70·1	21·4	48·7	0·9475	0·935	61·8	57·8	4·0
0·450	0·402	68·6	27·6	41·0	0·973	0·9575	61·5	58·9	2·6
0·461	0·412	68·5	28·2	40·3	1·000	1·000	61·0	61·0	0·0
0·6225	0·585	66·7	39·0	27·7					

Total and partial pressures have also been determined for the system benzene–ethylene dichloride (Table 7). A close approximation to Raoult's law is found, as is the case at 50° (Zawidski, *Z. physikal. Chem.*, 1900, **35**, 129).

The calculations above for the benzene–acetic acid system are based on Schmidt's vapour-pressure data (*ibid.*, **1926**, **121**, 221). Although these have been criticised (Hovorka and Dreisbach, *loc. cit.*), a smoothed curve plotted in terms of dimeric acetic acid seemed adequate for the present purpose.

We acknowledge with gratitude the gifts of chemicals from Imperial Chemical Industries, Limited, of charcoal from Messrs. Sutcliffe, Speakman, Ltd., and of beryllium–copper springs from Messrs. Instrument Specialities Co. Inc., of New Jersey. We are also grateful to Imperial Chemical Industries, Limited, for the loan of apparatus, and to The Distillers Co. Ltd., for a grant to the Department, which made this work possible.

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UNIVERSITY COLLEGE, HULL. [*Received, December 4th*, 1951.]

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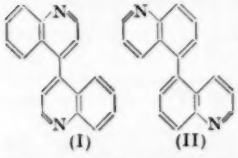
793. *The Optical Resolution of* 4 : 4′- *and* 5 : 5′-*Diquinolyl.*

By MALCOLM CRAWFORD and I. F. B. SMYTH.

4 : 4′- and 5 : 5′-Diquinolyl have been resolved into optically active forms which racemise readily in solution at room temperature.

The overlapping of the van der Waals radii of the intefering hydrogen atoms appears to be largely responsible for the stability of the isomers.

BELL and WARING (*J.*, 1949, 1579) showed that 1 : 1′-dianthryl exist in enantiomorphous forms, and later Bell, Morgan, and Smyth (*Chem. and Ind.*, 1951, 634) succeeded in resolving its 5 : 5′-dicarboxylic acid. Negative results had previously been obtained by Bell and Morgan (*J.*, 1950, 1963) with naphthidine, 1 : 1′-dinaphthyl-4 : 4′-dicarboxylic acid, and 8 : 8′-diquinolyl. The last compound, however, is not truly analogous to 1 : 1′-dinaphthyl as it lacks two hydrogen atoms in blocking positions, but this does not apply to 4 : 4′-diquinolyl (I) and 5 : 5′-diquinolyl (II), which were accordingly examined, and their resolutions briefly noted (*Chem. and Ind.*, 1951, 634).



(I) (II)

It is not clear just how closely the analogy between quinoline and naphthalene may be drawn, but it may be assumed for the present purpose that their structures do not differ significantly. Electron-diffraction studies have shown that for pyridine (Schomaker and Pauling, *J. Amer. Chem. Soc.*, 1939, **61**, 1769) the C–N bond length is 1·37 ± 0·03 Å and C–C 1·39 Å. If these lengths apply also to quinoline, it will differ very little from naphthalene.

There are two further uncertainties in making scale diagrams of the diquinolyls—the radius of the hydrogen atom and the interannular bond length. The former may have a value between 0·30 Å and 0·37 Å (Syrkin and Dyatkina, "Structure of Molecules," Butterworth, London, 1950, p. 190) and the latter between 1·48 Å, the interannular bond length in diphenyl, and 1·54 Å, the aliphatic C–C distance.

In a scale diagram, drawn by using the value 1·48 Å for the interannular bond length, there is only slight interference between the *ortho* and the *peri* hydrogen atom, when 0·37 Å is taken as the radius of the hydrogen atom but with the value 0·30 Å there is no interference at all. Similarly with 1·54 Å as the interannular bond length there is reduced interference when the hydrogen radius is taken as 0·37 Å and none when it is 0·30 Å. Calculations show that, when the interannular bond length is taken as 1·48 Å, the overlap of the hydrogen atoms of radius 0·37 Å is only 0·22 Å, but when the bond length is 1·54 Å, the overlap is reduced to 0·16 Å.

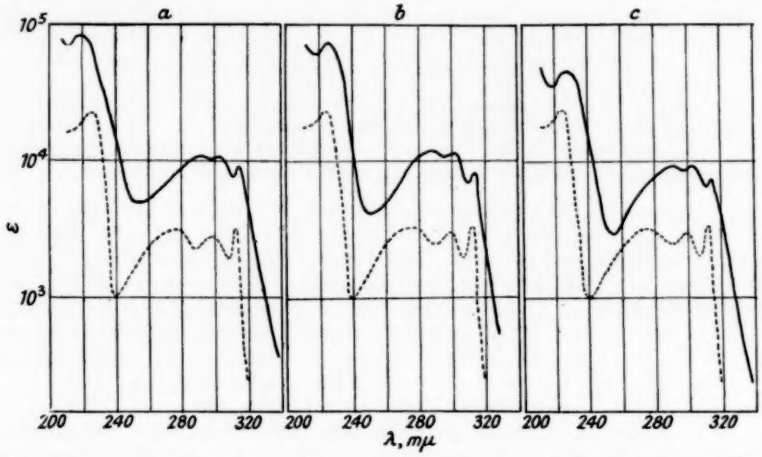
The value 1·48 Å for the interannular bond length applies when resonance occurs between the rings, as in diphenyl. This involves coplanarity of the ring systems. The value 1·54 Å is assumed when there is sufficient interference between the *ortho* and the *peri* substituent to render the rings non-coplanar. The interference in either case is so slight that it would hardly be expected to restrict rotation seriously. In spite of this 4 : 4′- and

5 : 5′-diquinolyl have been obtained in optically active forms, but their ease of racemisation effectively precludes the isolation of the pure isomers at ordinary temperatures.

When alcoholic solutions of 4 : 4′-diquinolyl and (+)-tartaric acid were mixed, a (+)-tartrate was obtained as very pale yellow prisms, m. p. 167—169°. Decompostion of this salt with ammonia at 0° gave the free base, which had an initial rotation of $[\alpha]_D^{17\cdot5}$ +205°. Treatment of the alcoholic filtrate with ammonia at 0° furnished active 4 : 4′-diquinolyl, $[\alpha]_D^{18}$ −52·3°.

The rotation of the solutions in N-hydrochloric acid fell fairly rapidly at room temperature, racemisation being virtually complete after 24 hours. Calculation from the rate of racemisation gave a half-life of about 2·5 hours at room temperature.

The mixing of alcoholic solutions of 5 : 5′-diquinolyl and (+)-tartaric acid gave a less soluble salt, which, on decomposition with ice-cold ammonia furnished the free base, $[\alpha]_D^{20\cdot5}$ +8·54°. Treatment of the mother liquors with ammonia gave 5 : 5′-diquinolyl, $[\alpha]_D^{20}$ −3·24°. The solutions in N-hydrochloric acid lost their activities at room temperature; the half-life period was 1·3 hours at room temperature.



Ultra-violet absorption spectra of (a) 4 : 4′-*diquinolyl* [$\lambda_{max.}$, mμ ($\varepsilon_{max.}$): 220 (80,200), 293 (10,650), 302 (10,550), *and* 316 (8630)], (b) 5 : 5′-*diquinolyl* [230 (69,200), 290 (11,800), 302 (11,000), and 315 (8230)], *and* (c) 8 : 8′-*diquinolyl* [230 (45,000), 295 (9340), 302 (9060), *and* 315 (7220), *compared in each case with that of quinoline*) (– – – – – –) [226 (22,900), 275 (3240), 299 (2890), *and* 312 (3320) (Albert, Brown, and Cheeseman, *J.*, 1951, 478); 235 (35,000), 278 (3500), 300 (2600), *and* 314 (3000) (Hearn, Morton, and Simpson, *J.*, 1951, 3327)].

The ultra-violet spectra of 4 : 4′- and 5 : 5′-diquinolyl (Figs. *a* and *b*) do not differ appreciably from that of quinoline (Albert, Brown, and Cheeseman, *J.*, 1951, 478, see also Hearn, Morton, and Simpson, *J.*, 1951, 3326) except in intensity of absorption. This result is expected in view of the observed optical activity of these compounds, since, with such double and single molecules, the ultra-violet spectra are similar generally where there is restricted rotation but quite different where there is coplanarity. It is therefore of interest that the ultra-violet absorption spectrum of 8 : 8′-diquinolyl (Fig. *c*) is very similar to those of 4 : 4′- and 5 : 5′-diquinolyl. This suggests that resonance between the rings is inhibited and hence that the quinoline residues are non-coplanar.

This does not mean, however, that the compound is resolvable. Kistiakowsky and Smith (*J. Amer. Chem. Soc.*, 1936, **58**, 1045) have shown that with molecules of the diphenyl type the energy required to bend the bonds and overcome repulsions of non-bonding atoms should be greater than 20 kcals. before resolution into optically active forms is possible. The two halves of the molecule may be normally non-coplanar, as indicated by the ultra-violet absorption spectrum, yet be so easily rotated about the bond holding them together that resolution, at least at ordinary temperatures, is out of the question.

The figure compares the ultra-violet spectra of 4 : 4′-, 5 : 5′-, and 8 : 8′-diquinolyl with

that of quinoline. There is a marked similarity throughout which indicates non-coplanarity. It seems unlikely that this is due to interference between the covalent shells of the hydrogen atoms concerned; the overlap is too small. The only likely alternative is that the larger overlap of the van der Waals envelopes is responsible for the hindrance to free rotation.

It is therefore not always necessary for the atoms themselves (*i.e.*, that part within the atomic radius) to overlap, although this is most effective in hindering rotation; it is sufficient, at least in some cases, if the van der Waals envelopes overlap, and these are to be considered of importance in stereochemical problems and possibly in steric effects generally.

Experimental

(M. p.s are uncorrected.)

The Resolution of 4 : 4′-*Diquinolyl.*—The compound, prepared by Clemo and Perkin's method (*J.*, 1924, 1608), formed crystals, m. p. 171°, from light petroleum (b.p. 60—80°) (Clemo and Perkin give m. p. 166°). Crystalline salts with (+)-camphorsulphonic and (+)-mandelic acids could not be obtained.

4 : 4′-Diquinolyl (0·44 g.) in boiling ethanol (2·8 ml.) was treated with a solution of (+)-tartaric acid (0·26 g.) in boiling ethanol (2·0 ml.). The filtered solution during 1 hour deposited a (+)-*tartrate* (0·22 g.) as pale yellow prisms, m. p. 167—169° (Found: C, 68·3; H, 4·5; N, 7·2. $C_{22}H_{18}O_6N_2$ requires C, 65·0; H, 4·5; N, 6·9%). The filtrate was treated at once with ice and ammonia solution; the base thus obtained was optically active, having α_D −2·25° (*c*, 4·30, *l* = 1, in N-hydrochloric acid) whence $[\alpha]_D^{18}$ −52·3°. The rotation of the solution diminished rapidly at room temperature:

Time, hours	1·0	1·7	2·0	3·0	4·0	5·0	6·0	7·0	8·0	20
$-\alpha_D$	2·25	1·75	1·64	1·25	1·03	0·75	0·58	0·44	0·31	0

The (+)-tartrate which contains one mole of base to one of acid, was decomposed with ice and ammonia solution, giving the base (m. p. 169—170°) (Found: C, 83·5; H, 4·7. Calc. for $C_{18}H_{12}N_2$: C, 84·4; H, 4·7%), α_D +11·15° (*c*, 5·44, *l* = 1, in N-hydrochloric acid), whence $[\alpha]_D^{17·5}$ +205°. It racemised at room temperature:

Time, hours	0·33	0·67	1·0	1·5	2·0	2·5	3·0	3·5	4·5
$+\alpha_D$	11·15	10·29	9·59	8·60	7·64	6·80	6·04	5·32	4·20
Time, hours	5·5	6·5	7·5	8·5	9·5	10·5	11·5	24	
$+\alpha_D$	3·27	2·55	1·97	1·51	1·17	0·89	0·69	0	

The Resolution of 5 : 5′-*Diquinolyl.*—This diquinolyl (Kozo Ueda, *J. Pharm. Soc. Japan*, **1931, 51,** 48; **1937, 57,** 180; see also Busch and Schmidt, *Ber.*, 1929, **62,** 2612) formed needles, m. p. 173—174°, from benzene–light petroleum. (+)-Camphorsulphonic acid and (+)-mandelic acid did not give crystalline salts. 5 : 5′-Diquinolyl (2·50 g.) in boiling ethanol (16 ml.) was treated with (+)-tartaric acid (1·48 g.) in boiling ethanol (14 ml.); the filtered solution during 15 minutes deposited (+)-*tartrate* (2·35 g.) as crystals, m. p. 204° (decomp.) (Found: C, 65·1; H, 4·5; N, 6·9. $C_{22}H_{18}O_6N_2$ requires C, 65·0; H, 4·5; N, 6·9%). The filtrate was treated at once with ice and ammonia solution, and gave a base which was examined polarimetrically without delay. It had a slight but definite activity, α_D −0·07° (*c*, 1·08, *l* = 2, in N-hydrochloric acid), whence $[\alpha]_D^{20}$ −3·24°. The rotation fell to zero in about 3 hours.

The salt, m. p. 204°, which contains one mole of base to one mole of acid, was decomposed by triturating it with ice and ammonia solution. The free base, m. p. 164—166° (Found: C, 81·4; H, 4·6; N, 10·5. Calc. for $C_{18}H_{12}N_2$: C, 84·4; H, 4·7; N, 10·9%) so obtained had α_D +0·15° (*c*, 5·89, *l* = 2, in N-hydrochloric acid), whence $[\alpha]_D^{20·5}$ +1·3°. Racemisation took place at room temperature:

Time, hours	0·25	0·75	1·1	1·75	2·75	4·75	18·75
α_D	0·15	0·12	0·09	0·06	0·04	0·02	0

The authors are indebted to Mr. M. St.C. Flett of the Research Department, Dyestuffs Division, Imperial Chemical Industries Limited, for the determination of ultra-violet absorption spectra, and also express their thanks to Professor F. Bell who suggested the topic.

College of Technology, Belfast. [*Received, March 20th,* 1952.]

794. *The Reaction between Aromatic Compounds and Derivatives of Tertiary Acids. Part VII.* The Production of* p-tert.-*Butylphenyl and* iso*But*-1-*enyl* tert.-*Butyl Ketones from Pivaloyl Chloride.*

By Michael E. Grundy, Wei-hwa Hsü, and Eugene Rothstein.

The formation of *tert.*-butyl *p-tert.*-butylphenyl ketone when pivaloyl chloride is slowly added to a mixture of benzene and aluminium chloride (Pearson, *J. Amer. Chem. Soc.*, 1950, **72**, 4169) results from the reaction between *p-tert.*-butylbenzene, which is the first product, and the acid chloride (compare Rothstein and Saville, Part II, *J.*, 1949, 1950). The diminution of the first-order velocity constant in the course of the reaction (*idem*, Part III, *ibid.*, p. 1954) which occurs even in the absence of benzene is now shown to be due to *iso*but-1-enyl *tert.*-butyl ketone. This ketone is formed by condensation of *iso*butylene (arising from the decomposition of pivaloyl chloride) with unchanged pivaloyl chloride; when it is added to a Friedel–Crafts reaction mixture it completely deactivates the catalyst and thus prevents all further reaction.

It was noted in Part III (*J.*, 1949, 1954) that the rate of disappearance of pivaloyl chloride when mixed with aluminium chloride diminished appreciably towards the end of the reaction, *i.e.*, the curve formed by a plot of the logarithm of the concentration against time tended to flatten out towards the time axis. Since then, even more marked examples of the phenomenon have been encountered, notably when solutions of the acid halide in pure nitrobenzene were used. In such cases the reaction, which initially is very rapid, soon ceases and proceeds to a limited extent only if a further quantity of catalyst is added. Neither addition of more acid chloride nor dilution of the solvent with benzene will restart the reaction (details will be given in a later communication). It proceeds normally if it is catalysed by the pre-formed complex of aluminium chloride and nitrobenzene provided that the latter is only a small proportion of the total solvent. The reason therefore for the deactivation of the aluminium chloride is evidently the rapid formation of a by-product with which it forms a stable compound.

The foregoing largely invalidates the explanation offered by Wertyporoch and Adamus (*Z. physikal. Chem.*, 1934, **168**, 38) for the inactivity of nitrobenzene solutions of aluminium halides towards alkyl and acyl halides. They considered that the very stable complex formed by the solvent with the catalyst was responsible for the ineffectiveness of the latter. This, however, is inconsistent with the normal catalytic activity shown when a solution of the complex is added to a mixture of an acyl halide and benzene. The non-reactivity of nitrobenzene evidently should be ascribed to the deactivation of the benzene nucleus, and this is doubtless true for the results Wertyporoch *et al.* obtained for halogen-substituted benzene as well.

The necessity for using more than one molecule of aluminium chloride in Friedel–Crafts acylation reactions is of course due to progressive loss of catalytic efficiency as a result of compound formation with the product (see also Part IV, *J.*, 1949, 1959). Recently, Pearson (*J. Amer. Chem. Soc.*, 1950, **72**, 4169) reported a yield of over 46% of *tert.*-butylpivalophenone † (*tert.*-butyl *tert.*-butylphenyl ketone, $CMe_3 \cdot C_6H_4 \cdot CO \cdot CMe_3$) when pivaloyl chloride was *slowly* added during 20—60 minutes to a stirred mixture of aluminium chloride and benzene. In this case it is quite clear that primarily *tert.*-butylbenzene is formed and that further reaction furnishes the ketone, provided that the acid chloride is added slowly enough. If the addition is in one portion the 87% yield of carbon monoxide (Part II, *loc. cit.*) shows that hydrocarbon must be the main product. The substitution of *tert.*-butylbenzene for benzene as the solvent reduced the yield of carbon monoxide to 65% and correspondingly the ketone was isolated in 26·3% yield. Acylation is thus particularly sensitive to changes both in solvent (none occurred when a carbon disulphide solution of *tert.*-butylbenzene was used) and in concentration (unpublished work). It

* Part VI, *J.*, 1951, 1459.

† Recalculated on the basis of acid chloride employed. For reasons given in Part II we do not consider that yields calculated on the final products isolated are reliable.

would be perhaps over-simplification to assume that the sole factor is the slow addition of pivaloyl chloride which then allows the *tert.*-butylbenzene to be further acylated, but, on using the condition described by Pearson and varying the time of addition, there is a variation in the yield of ketone (as shown below) though in no case was it quite as high as that obtained by him.

Time of addition, min.	20	45	50
Yield of ketone, %	16*	32·5	36·9

* Yield of CO, approx. 84%.

The gradual accumulation of this ketone would undoubtedly slow down the main reaction, especially in cases where the molecular concentration of aluminium chloride was low compared to the concentration of the acid chloride. A ratio of 1 : 10 was used in the kinetic experiments described in Part III. However, no *tert.*-butylpivalophenone was ever detected in these dilute solutions and, further, neither in carbon disulphide nor in nitrobenzene solution is its formation possible.

Although Pearson reported that there was no product when he repeated his reaction in nitrobenzene, it appeared to us that his experiments were inadequate. It was found, for example, that, when the reactants were mixed, a proportion of the acid chloride rapidly disappeared, and in these particular experiments there was an accompanying evolution of carbon monoxide amounting to about 10% of that theoretically possible. Now the first product in the decomposition of pivaloyl chloride is *iso*butylene (Boëseken, *Rec. Trav. chim.*, 1910, **24**, 85), which usually polymerises, but neither *iso*butylene nor its polymer hinders the subsequent reaction, and consequently it was desirable to search for some other substance, probably of a ketonic nature. Fractionation afforded an unsaturated ketone, $C_9H_{16}O$, b. p. 58°/15 mm. (semicarbazone, m. p. 119—120°), possessing the expected inhibitory action when added to aluminium chloride. The most likely structures suggesting themselves were *iso*but-1-enyl *tert.*-butyl ketone (I) and *tert.*-butyl 2-methylallyl ketone (II) both of which can result from reaction between *iso*butylene and pivaloyl chloride :

$$CMe_2{:}CH_2 + Cl{\cdot}CO{\cdot}CMe_3 \longrightarrow \underset{(I)}{CMe_2{:}CH{\cdot}CO{\cdot}CMe_3} \text{ or } \underset{(II)}{CH_2{:}CMe{\cdot}CH_2{\cdot}CO{\cdot}CMe_3}$$

Less likely possibilities were hexamethyldiacetyl and hexamethylacetone, both of which were synthesised in order to make a direct comparison. Neither of these yielded semicarbazones, and the boiling points of both were substantially different from that of the above ketone.

The reaction leading to (I) and (II) is very similar to the production of mesityl oxide from *iso*butylene and acetyl chloride with zinc chloride as catalyst (Kondakov, *J. Russ. Phys. Chem. Soc.*, 1894, **26**, 5), or to the formation of a β-chloro-ketone by addition of acetyl chloride to trimethylethylene, which is then followed by elimination of hydrogen chloride (Wieland and Bettag, *Ber.*, 1922, **55**, 2246). Some confirmation was obtained in that when *iso*butylene was mixed with pivaloyl chloride and aluminium chloride in carbon disulphide solution the unsaturated ketone was isolated in 20% yield. Its independent synthesis from 2-methylbut-2-enoyl chloride, as below, confirmed it to be the *iso*butenyl ketone.

$$CMe_2{:}CH{\cdot}COCl + Cl{\cdot}Mg{\cdot}CMe_3 \longrightarrow CHMe_2{:}CH{\cdot}CO{\cdot}CMe_3$$

Experimental

The reaction between pivaloyl chloride and benzene was carried out as nearly as possible as described by Pearson (*loc. cit.*), except that the times of addition were measured more exactly. These times were (i) 20, (ii) 45, and (iii) 50 minutes. The products were : (i) Approx. vol. of carbon monoxide 1488 c.c.; *tert.*-butylbenzene, b. p. 58°/15 mm., 3·36 g. (33·6%); *tert.*-butyl *tert.*-butylphenyl ketone, b. p. 147°/12 mm., 2·79 g. (17%) (Found : C, 82·7; H, 10·1. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%) [oxime, m. p. 205° (Found : C, 77·1; H, 9·6; N, 6·3. Calc. for $C_{15}H_{23}ON$: C, 77·2; H, 9·9; N, 6·0%)]. (ii) *tert.*-Butylbenzene, 1·7 g. (17%); ketone, 5·3 g. (32·5%). (iii) *tert.*-Butylbenzene, 0·85 g. (8·5%); ketone, 6·02 g. (37%).

Preparation of But-1-enyl tert.*-Butyl Ketone.*—(a) *From pivaloyl chloride.* A solution of pivaloyl chloride (24·2 g., 0·2 mol.) in nitrobenzene (50 c.c.) was slowly added to freshly distilled aluminium chloride (14 g., 0·105 mol.) dissolved in the same solvent (100 c.c.) and cooled to 0°. After 1 hour's stirring, more aluminium chloride (7 g., 0·055 mol.) in nitrobenzene (30 c.c). was added, and after another hour the liquid was warmed to 40—50° for 0·5 hour. The product

was decomposed with ice and 10% hydrochloric acid, the organic layer separated, and an ethereal extract of the aqueous layer added to it. The combined layers were dried (Na_2SO_4). Fractionation afforded iso*but*-1-*enyl* tert.-*butyl ketone* (4·5 g., 20%), b. p. 58°/15 mm. (Found: C, 77·1; H, 11·9%; *M*, 142. $C_9H_{16}O$ requires C, 77·1; H, 11·4%; *M*, 140). The *semicarbazone*, prepared in pyridine, separated from water in needles, m. p. 119—120° (Found: C, 61·2; H, 9·6; N, 21·3. $C_{10}H_{19}ON_3$ requires C, 60·9; H, 9·6; N, 21·3%).

(b) *From* iso*butylene*. The gas generated from *tert.*-butyl alcohol by the action of 30% sulphuric acid (Barkenbus and Kelly, *J. Chem. Educ.*, 1945, **22**, 356) was passed for 1 hour into a carbon disulphide (100 c.c.) solution of pivaloyl chloride (12 g., 0·1 mol.) at −12°. Whilst the passage of the *iso*butylene was continued, aluminium chloride (26 g., 0·2 mol.) was added from a dropping tube, the temperature being kept between −12° and −20°. More acid chloride (3 g.) was added, and the temperature then allowed to rise gradually to that of the room. Initially there was a vigorous reaction, and towards the end oily drops of polymerised *iso*butylene separated. After decomposition with ice and subsequent extraction, the product was fractionated, yielding, together with other material including unchanged pivalic acid, polymerised product, etc., the above ketone (2·2 g.) (Found: C, 77·0; H, 12·2%). The semicarbazone, which appeared to be identical (m. p. and mixed m. p.) with that noted above, also gave rather poor analytical figures (Found: C, 60·4; H, 8·7; N, 20·6%).

(c) *From* 2-*methylbut*-2-*enoyl chloride*. The acid (*Org. Synth.*, 1943, **23**, 27) was converted into the acid chloride with thionyl chloride (Schindler and Reichstein, *Helv. Chim. Acta*, 1942, **25**, 551), the yield of product, b. p. 145—150°, being 90%. An ethereal (50 c.c.) solution of the acid chloride (12 g., 0·1 mol.), containing quinol (0·1 g.), was slowly added to a stirred solution in ether of *tert.*-butylmagnesium chloride prepared from *tert.*-butyl chloride (12 g.) and magnesium (2·5 g.). The liquid was warmed for 30 minutes on the steam-bath and then decomposed with ice. The ketone, b. p. 58°/15 mm., was obtained in 14% yield (2 g.), together with unchanged acid and some undistillable tar. The semicarbazone was identical (m. p. and mixed m. p.) with that obtained from the product of the Friedel–Crafts reactions (*a*) and (*b*) (Found: C, 60·8; H, 9·6; N, 21·2%).

Preparation of Hexamethyldiacetyl.—This was prepared by a method similar to that used by Mushenko (*Chem. Abs.*, 1943, **37**, 5697), pivaloyl chloride being substituted for the bromide. A mixture of pivaloyl chloride (12 g.), " molecular " sodium (3 g.), and ether (100 c.c.) furnished approximately 4 g. of the pure ketone, b. p. 168°. It did not afford a semicarbazone.

Preparation of Hexamethylacetone.—Only a poor yield of the ketone (b. p. 153°) was obtained by reaction of pivaloyl chloride with acetone (Whitmore, *Rec. Trav. chim.*, 1938, **57**, 566). Better yields resulted from the condensation of methyl pivalate (Richard, *Ann. Chim.*, 1910, **21**, 335) with *tert.*-butyl chloride in the presence of sodium, and oxidation of the mixture of di-*tert.*-butylcarbinol and hexamethylacetone with concentrated nitric acid (Bartlett and Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 141). A semicarbazone could not be obtained.

Friedel–Crafts Reaction with iso*But*-1-*enyl* tert.-*Butyl Ketone.*—The ketone (0·7767 g.) was mixed with nitrobenzene (140 c.c.) and to this were added first a solution of freshly prepared aluminium chloride (0·6320 g.) in nitrobenzene (20 c.c.) and then pivaloyl chloride (5·6664 g.) in the same solvent (20 c.c.). There was no reaction and no carbon monoxide was evolved.

THE UNIVERSITY, LEEDS. [*Received, June 9th*, 1952.]

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795. *The Chlorostannates of Hydrazine and 3 : 5 : 5-Trimethylpyrazoline.*

By W. PUGH and A. M. STEPHEN.

Dihydrazinium chlorostannate has been prepared and shown to form compounds with simple aliphatic ketones. Monohydrazinium chlorostannate, although reported in the literature, appears not to exist. Condensation of acetone with stannic chloride and hydrazine dihydrochloride yields bis-3 : 5 : 5-trimethylpyrazolinium chlorostannate containing 1·5 mols. of acetone of crystallisation; the acetone-free salt is best prepared by a more direct method.

DRUCE (*Chem. News*, 1922, **124**, 310) prepared a series of diamine stannichlorides and reported a substance formulated as N_2H_4,H_2SnCl_6 (probably more correctly $N_2H_6SnCl_6$), this being the only chlorostannate of hydrazine in the literature. This formulation,

although in harmony with that of the chlorostannates of ethylenediamine and phenylenediamine, prepared also by Druce and confirmed in this laboratory, nevertheless appears to be an unusual one for a compound of hydrazine, which forms a well-known series of salts containing the univalent hydrazinium ion ($N_2H_5^+$); furthermore, the substance was made from stannic chloride and hydrazine monohydrochloride, a procedure which might be expected to yield dihydrazinium chlorostannate, $(N_2H_5)_2SnCl_6$.

This preparation has accordingly been repeated by use of stannic chloride and varying amounts of hydrazine mono- or di-hydrochloride, but the only product isolated is dihydrazinium chlorostannate. Furthermore, if such a compound as reported by Druce does exist, it might be expected to result from the direct union of hydrazine dihydrochloride and anhydrous stannic chloride; combination does not in fact take place when these substances are heated, whereas hydrazine monohydrochloride reacts vigorously with stannic chloride to give the expected dihydrazinium chlorostannate. In view of the catalytic decomposition of hydrazine salts, especially by platinum yielding ammonia (Audrieth and Ogg, "The Chemistry of Hydrazine," Wiley, 1951, p. 145), it is possible that Druce's product contained ammonium chlorostannate which contains tin and chloride in proportions very similar to the analytical figures given (the hydrazine content was not reported). Our preparations were made in glass vessels and none of them contained more than 0·1% of ammonia.

Dihydrazinium chlorostannate is not easy to obtain pure by crystallisation, for the hydrochlorides tend to separate with it, particularly from hydrochloric acid solution. Fractional crystallisation is usually necessary, though a reasonably pure product can be obtained from aqueous solutions containing less than the theoretical amount of hydrazine monohydrochloride. The best method is to crystallise from aqueous solutions containing small amounts of acetone, which seems to inhibit the separation of the hydrochlorides. Slow evaporation of a concentrated solution of dihydrazinium chlorostannate containing acetone of crystallisation, described below, yields flawless crystals suitable for *X*-ray crystallography.

Whereas the chlorostannate is obtained from water in the anhydrous condition, it is remarkable that it separates from aqueous ketones with ketone of crystallisation; *e.g.*, acetone–water solutions (1 : 1) yield particularly well-formed crystals, resembling Iceland spar, which contain 3 mols. of acetone per mol. of chlorostannate. The number of mols. of ketone accommodated by the crystal diminishes, however, as the molecular weight of the ketone rises; *e.g.*, the compounds with ethyl methyl ketone, diethyl ketone, and di-*n*-propyl ketone all contain 1·5 mols. of ketone per mol. of chlorostannate, and di*iso*propyl ketone does not form a compound at all. In the dry state these compounds are very stable, no loss in weight occurring when the acetone and diethyl ketone compounds are heated for several hours *in vacuo* at 112°. On the other hand, the ketones are liberated immediately the compounds are dissolved in water.

Although acetone does not condense with dihydrazinium chlorostannate when heated under reflux, condensation does occur with hydrazine dihydrochloride and stannic chloride, colourless cubes being deposited from a deep maroon-coloured liquor in the course of 2—3 hours. The product (m. p. 218°), obtained in 90% yield, has been shown to be bis-3 : 5 : 5-trimethylpyrazolinium chlorostannate containing 1·5 mols. of acetone, the heterocyclic base, characterised as its hydrochloride, being isolated by decomposition with alkali and extraction with ether. This substituted pyrazoline is the expected product whether the reaction proceeds by condensation of hydrazine with mesityl oxide formed *in situ* from acetone or by the formation of dimethylketazine and subsequent isomerisation in presence of acid (Frey and Hoffmann, *Monatsh.*, 1901, **22**, 760). Diethyl ketone is insufficiently reactive to give a pyrazolinium derivative when substituted for acetone in this reaction.

Acetone is removed from this compound by dissolving it in alcohol and precipitation with ether, or by long storage in chloroform, though not by heating *in vacuo* at 100°. Bis-3 : 5 : 5-trimethylpyrazolinium chlorostannate is prepared more conveniently, however, by mixing 3 : 5 : 5-trimethylpyrazoline hydrochloride and excess of stannic chloride in alcohol and adding ether. The product readily adds 1·5 mols. of acetone per mol. of chlorostannate, but does not form compounds with ethyl methyl ketone or diethyl ketone under similar conditions.

It is hoped that an examination of the crystal structures of some of these compounds, at present in progress in the Physics Department of this University, will throw some light on the mode of linking of the ketone.

Experimental

M. p.s are uncorrected. Analyses were made by standard methods: hydrazine and chloride by Andrews's and Volhard's methods, respectively, tin by precipitation with ammonia (Hillebrand and Lundell, "Applied Inorganic Analysis," Wiley, 1929, p. 239), and ketones by precipitation with 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid (the chlorostannates of hydrazine and 3 : 5 : 5-trimethylpyrazoline were shown not to interfere).

Preparation of Dihydrazinium Chlorostannate.—(*a*) Stannic chloride pentahydrate (25·6 g.) and hydrazine monohydrochloride (9 g.) were dissolved in water (20 c.c.), and the clear solution was evaporated slowly over sulphuric acid. The first two crops of *dihydrazinium chlorostannate* (8 g.) were separated on a sintered-glass funnel, washed with ethanol and ether, and dried in air (Found: N_2H_4, 17·5; Cl′, 53·0; Sn, 27·2%). The next crop (12 g.) was washed instead with ice–water (considerable loss) and dried, first on filter-paper and then over sulphuric acid [Found: N_2H_4, 15·9; Cl′, 53·3; Sn, 29·5. $(N_2H_5)_2SnCl_6$ requires N_2H_4, 16·1; Cl′, 53·3; Sn, 29·85%]. Washing with ethanol and ether thus causes decomposition with the removal of a disproportionate amount of stannic chloride. When an excess of hydrazine monohydrochloride or when the dihydrochloride was used, or when hydrochloric acid was added, the chlorostannate crystals were contaminated with hydrochloride. Crystallisation from hot solutions had the same effect.

(*b*) Anhydrous stannic chloride (3 c.c.) was distilled on to hydrazine monohydrochloride (1 g.); there was a considerable heat of reaction. The mixture was refluxed for 5 minutes, and excess of stannic chloride was then removed in a current of dry air. The increase in weight and analysis of the product indicated 80% conversion of the monohydrochloride into chlorostannate. The product was finely ground and treated again in the same manner, yielding a white crystalline powder (Found: N_2H_4, 15·8; Cl′, 53·5%).

Properties of Dihydrazinium Chlorostannate.—The salt crystallises as transparent tetragonal needles. It sublimes with decomposition when heated gently in a current of nitrogen, the sublimate containing mostly ammonium salts and only a trace of hydrazine; rapid heating to a higher temperature affords a yellow oil just below red heat. The salt is insoluble in ether, benzene, chloroform, and carbon tetrachloride, but soluble in hot methanol and ethanol (from which hydrazine monohydrochloride is deposited on cooling) and exceedingly soluble in water. Concentrated aqueous solutions remain clear when kept, but dilution causes precipitation of gelatinous tin hydroxide. Solutions in simple aliphatic ketones or in ketone–water mixtures afford compounds containing ketone of crystallisation.

Reactions of Dihydrazinium Chlorostannate.—(*a*) *With acetone.* Crystallisation of the chlorostannate (or a mixture of hydrazine monohydrochloride and stannic chloride in equivalent quantities) from water–acetone (1 : 1) yielded large clear rhombs, m. p. 137—138°, of solvated *chlorostannate* [Found: N_2H_4, 11·25; Cl′, 37·2; Sn, 20·8. $(N_2H_5)_2SnCl_6,3C_3H_6O$ requires N_2H_4, 11·2; Cl′, 37·2; Sn, 20·8%]. The presence of the acetone was established by formation of its 2 : 4-dinitrophenylhydrazone (m. p. and mixed m. p. 127°) in 96% of the theoretical yield.

(*b*) *With ethyl methyl ketone.* This *compound* could only be prepared in the absence of water. Dihydrazinium chlorostannate (3 g.) dissolved in the ketone (3 c.c.) with evolution of heat, forming a viscous liquid which failed to crystallise. When this was shaken with ether (10 vols.) two phases separated and crystallisation then occurred during several days at 0°, yielding large clear tetragonal prisms, m. p. 90° [Found: N_2H_4, 12·7; Cl′, 42·1; Sn, 23·3; C_4H_8O, 21·2. $(N_2H_5)_2SnCl_6,1{\cdot}5C_4H_8O$ requires N_2H_4, 12·65; Cl′, 42·0; Sn, 23·5; C_4H_8O, 21·45%]. The ethyl methyl ketone 2 : 4-dinitrophenylhydrazone formed from it had m. p. 112—113°, raised to 114° on admixture with an authentic specimen.

(*c*) *With diethyl ketone.* A solution containing stannic chloride pentahydrate (10·5 g.) and hydrazine monohydrochloride (4·1 g.) in water (10 c.c.) and diethyl ketone (5 c.c.) gave rectangular prisms, m. p. 155° (recrystallised from ethanol containing diethyl ketone) [Found: N_2H_4, 12·2; Cl′, 40·5; Sn, 22·4; $C_5H_{10}O$, 25·2. $(N_2H_5)_2SnCl_6,1{\cdot}5C_5H_{10}O$ requires N_2H_4, 12·15; Cl′, 40·4; Sn, 22·5; $C_5H_{10}O$, 24·5%]. The 2 : 4-dinitrophenylhydrazone of diethyl ketone, prepared from this *compound*, had m. p. and mixed m. p. 153°. Refluxing hydrazine dihydrochloride (2 g.) and stannic chloride (1 c.c.) in diethyl ketone (8 c.c.) for 6 hours gave as the major product, precipitated in the cold by ether, the above chlorostannate, m. p. 155°, and not a pyrazoline derivative (see below).

(*d*) *With di-*n*-propyl ketone.* Dihydrazinium chlorostannate (2 g.) was boiled with di-*n*-propyl ketone (3 c.c.). Most of it dissolved, leaving a small oily layer which crystallised on cooling (hydrazine monohydrochloride). When the solution was shaken with ether (6 vols.) the liquid separated into two layers and crystallised slowly at 0°, forming the *complex* in clear rhombs, m. p. 87—89° (decomp.) [Found: N_2H_4, 11·3; Cl′, 37·2; Sn, 20·7. $(N_2H_5)_2SnCl_6,1{\cdot}5C_7H_{14}O$ requires N_2H_4, 11·25; Cl′, 37·4; Sn, 20·9%]. The 2 : 4-dinitrophenylhydrazone prepared from this had m. p. 72°, undepressed by a specimen obtained from di-*n*-propyl ketone.

Bis-3 : 5 : 5-*trimethylpyrazolinium Chlorostannate.*—(*a*) Acetone (50 c.c.) containing hydrazine dihydrochloride (9 g., 0·086 mol.) and stannic chloride (5 c.c., 0·042 mol.) was heated under reflux for 3 hours, whereupon the hydrazine salt passed slowly into solution and the deep red liquid deposited yellowish cubic crystals (20 g.). Recrystallisation from hot ethanol containing acetone yielded *bis*-3 : 5 : 5-*trimethylpyrazolinium chlorostannate* with 1·5 mols. acetone of crystallisation, colourless cubes, m. p. 215—218° (decomp.) [Found, in material dried in air: N_2H_4, nil; N, 8·9; Cl′, 33·0; Sn, 18·5; C_3H_6O, 13·3. $(C_6H_{13}N_2)_2SnCl_6,1{\cdot}5C_3H_6O$ requires N, 8·7; Cl′, 33·0; Sn, 18·4; C_3H_6O, 13·5%]; the identification of this substance is described below.

When dihydrazinium chlorostannate was refluxed with acetone for 3 hours, the pyrazolinium compound was not formed. Instead, the product was dihydrazinium chlorostannate with acetone of crystallisation.

(*b*) 3 : 5 : 5-Trimethylpyrazoline, prepared by Kishner's method (*Chem. Zentr.*, 1912, I, 2025), was characterised as its *N*-benzoyl derivative, m. p. 238° (Frey and Hoffmann, *loc. cit.*, give 236°), hydrochloride, m. p. 175° (lit., 176°), and chloroplatinate, m. p. 185° (lit., 186°). The oxalate, needles, m. p. 131·5°, from ethanol–light petroleum (b. p. 75—90°), was analysed by Turrentine's method (*J. Amer. Chem. Soc.*, 1910, **32**, 577) (Found: N, 14·3; $H_2C_2O_4$, 44·1. Calc. for $C_6H_{12}N_2,H_2C_2O_4$: N, 13·9; $H_2C_2O_4$, 44·5%). Harries (*Annalen*, 1901, **319**, 233) gives m. p 148°. When acetone was added to 3 : 5 : 5-trimethylpyrazoline hydrochloride (0·7 g.) and stannic chloride (0·3 c.c.) in absolute ethanol (10 c.c.) acidified with hydrochloric acid, the chlorostannate separated with acetone of crystallisation as glistening, well-formed cubes, identical with the product, m. p. 215—218°, described above; the m. p. was raised to 221° (decomp.) by recrystallisation from methanol–acetone containing hydrochloric acid. When a large volume of ether was added to the pyrazoline hydrochloride (0·3 g.) and stannic chloride (0·16 c.c.) in ethanol, a colourless oil separated which when scratched afforded *bis*-3 : 5 : 5-*trimethylpyrazolinium chlorostannate* as microscopic prisms, m. p. 198° (decomp.) [Found, in material dried at 100° *in vacuo*: N, 10·0; Cl′, 38·0; Sn, 21·1. $(C_6H_{13}N_2)_2SnCl_6$ requires N, 10·0; Cl′, 38·2; Sn, 21·4%]. Addition of acetone to a concentrated solution of this compound in ethanol afforded the characteristic cubes, m. p. 221°, containing acetone of crystallisation, but no precipitate was obtained when ethyl methyl ketone or diethyl ketone was used in place of acetone.

Decomposition of the Chlorostannate (*m. p.* 218°) *with Alkali.*—The above compound (10 g.) was mixed into a paste with barium oxide (large excess) and water (10 c.c.), and solid potassium hydroxide (5 g.) was then added. After 30 minutes the mixture was extracted thoroughly with ether, and the ethereal extract dried (KOH) and distilled through a short column. The fraction, b. p. 156° (1·5 c.c.), was identified as 3 : 5 : 5-trimethylpyrazoline by formation of the hydrochloride, m. p. and mixed m. p. 177° (Found: N, 19·2. Calc. for $C_6H_{13}N_2Cl$; N, 18·9%).

The substance of this paper is to be read before Section A of the South African Association for the Advancement of Science at its meeting in Cape Town, July, 1952.

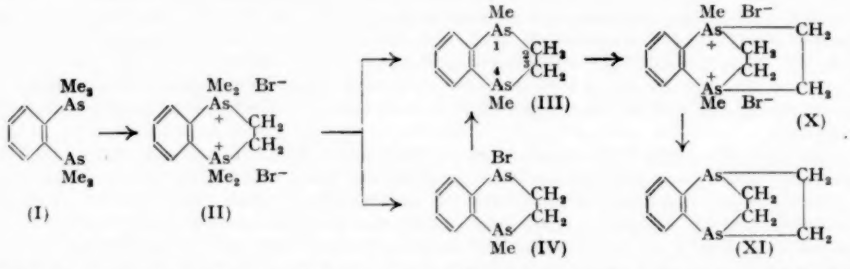
UNIVERSITY OF CAPE TOWN. [*Received, June 14th*, 1952.]

796. *The Preparation and Properties of* 1 : 4-*Dimethylethylene*-o-*phenylenediarsine and of Di-ethylene*-o-*phenylenediarsine.*

By Frederick G. Mann and F. C. Baker.

o-Phenylenebis(dimethylarsine) combines with ethylene dibromide to give 1 : 1 : 4 : 4-tetramethylethylene-*o*-phenylenediarsonium dibromide (II), which on thermal decomposition gives 1 : 4-dimethylethylene-*o*-phenylenediarsine (III) and 1-bromo-4-methylethylene-*o*-phenylenediarsine (IV). The 1 : 4-dimethyl-diarsine in turn combines with ethylene dibromide to give diethylene-*o*-phenylenediarsine dimethobromide (X), which on thermal decomposition gives diethylene-*o*-phenylenediarsine (XI). These three ditertiary arsines show remarkable similarity in their behaviour towards quaternising agents, which is in marked contrast to that of tri-*o*-phenylenediarsine.

The quaternisation of *o*-phenylenebisdimethylarsine (I), originally prepared by Chatt and Mann (*J.*, 1939, 610), shows certain features which are characteristic of the three ditertiary arsines studied in the present investigation. Earlier work (cf. Beeby and Mann, *J.*, 1951, 887) indicated that the diarsine (I) apparently formed only a monomethobromide and a monomethiodide. We find, however, that the diarsine when dissolved in cold methyl bromide readily forms a monomethobromide, m. p. 225—226°, but when heated with methyl bromide at 100° gives a dimethobromide, which decrepitates at *ca.* 150° and subsequently melts at 222—223°. Similarly a solution of the diarsine in an excess of methyl iodide, when boiled under reflux for several hours, forms only a monomethiodide, m. p. 228—230°, but when heated at 100° as before gives the dimethiodide, m. p. 222—224°. In each series, therefore, the quaternisation of the second arsine group requires much more vigorous conditions than that of the first group; moreover, the above melting points indicate that both the diquaternary salts readily lose one molecule of alkyl halide when heated, to give the more stable monoquaternary salts, and that the apparent melting point of each diquaternary salt is probably that of the residual monoquaternary salt.



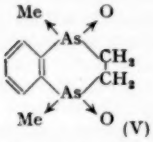
When however the diarsine (I) is heated with one molecular equivalent of ethylene dibromide at 125—130°, *i.e.*, just below the boiling point of the latter, diquaternisation readily occurs with the formation of 1 : 1 : 4 : 4-tetramethylethylene-*o*-phenylenediarsonium dibromide (II), systematically named 1 : 1 : 4 : 4-tetramethyl-1 : 2 : 3 : 4-tetrahydro-1 : 4-diarsonianaphthalene dibromide (Glauert and Mann, *J.*, 1950, 682). A similar derivative is obtained by using trimethylene dibromide. All the above quaternary salts of the diarsine (I) are colourless.

We have investigated in some detail the thermal decomposition of the dibromide (II). The course of this decomposition is markedly affected by the physical conditions employed, and also apparently by slight traces of impurities. When however the pure dry salt is rapidly heated in nitrogen at *ca.* 0·1 mm., the decomposition follows two courses, for the liquid distillate on refractionation yields 1 : 4-dimethylethylene-*o*-phenylenediarsine (III) and 1-bromo-4-methylethylene-*o*-phenylenediarsine (IV).

The diarsine (III) is a colourless liquid which on quaternisation behaves precisely as

does (I), *i.e.*, with an excess of methyl bromide in the cold it forms a monomethobromide but at 100° regenerates the dibromide (II), and with an excess of boiling methyl iodide forms a monomethiodide, but at 100° forms a dimethiodide. The dimetho-bromide and -iodide have, however, considerably greater stability than the corresponding salts of the diarsine (I), for they can be heated in a vacuum to at least 100° without loss of alkyl halide.

The diarsine (III) was readily oxidised by hydrogen peroxide to the diarsine dioxide (V), which was isolated as the bishydroxypicrate. It is notable however that whereas the diarsine (I) readily co-ordinates with palladous bromide to form the cyclic compound (VI) (Chatt and Mann, *J.*, 1939, 1622), the diarsine (III) gives a compound of composition $(C_{10}H_{14}As_2)_2PdBr_2$, in which only one arsenic atom in each molecule of the diarsine has co-ordinated with the palladium. This composition is undoubtedly determined primarily by the stereochemistry of the diarsine (III), the effect being probably reinforced by the greater reluctance of the second arsenic atom to increase its valency.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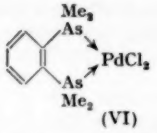
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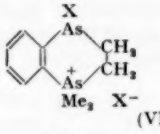
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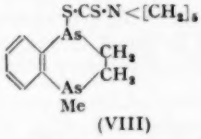

(VIII)

Although the above fractional distillation gave the pure diarsine (III), b. p. 106—108°/0·3 mm., the bromo-arsine (IV), b. p. 120°/0·3 mm., could not by these means be obtained entirely free from the diarsine. The identity of the bromoarsine (IV) rests, however, on the following evidence. A solution in an excess of methyl bromide when heated at 100° gave the colourless crystalline monomethobromide (VII; X = Br), and a similar solution in methyl iodide when boiled under reflux gave the deep yellow crystalline 1-iodo-4-methylethylene-*o*-phenylenediarsine monomethiodide (VII; X = I). The colour of this salt was a strong indication of an As–I link, and the presence of a similar As–Br link in the parent arsine (IV) was shown by the fact that the arsine reacted readily with piperidine *N*-pentamethylenedithiocarbamate to give the dithiourethane (VIII), the identity of which was confirmed by both analysis and molecular-weight determinations. It might be considered however that the above evidence does not distinguish decisively between the bromo-arsine (IV) and the compound (IX) which might conceivably arise from the thermal decomposition of (II) and would differ in composition from (IV) only by two hydrogen atoms. When however the bromo-arsine was treated with methylmagnesium iodide it gave the diarsine (III), which was characterised by its crystalline derivatives, whereas the compound (IX) would have given the original tetramethyldiarsine (I).

Once the two components (III) and (IV) of the original mixture arising from the thermal decomposition of (II) had been identified, refractionation was clearly unnecessary when only the diarsine (III) was required: for this purpose the crude distillate was treated with an excess of methylmagnesium iodide, and the product on distillation readily yielded the pure diarsine (III).

The diarsine (III), when in turn heated with one molecular equivalent of ethylene dibromide at 120—125°, gave the crystalline dimethobromide (X) of diethylene-*o*-phenylenediarsine; this salt when treated with ethanolic sodium picrate readily gave the corresponding dimethopicrate, thus proving that both bromine atoms in (X) were ionic, and that cyclisation by the second molecule of ethylene dibromide had actually occurred.

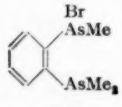
The dibromide (X), when heated under the conditions described for (II), also underwent a smooth thermal decomposition, giving a crude distillate which on careful fractionation gave pure diethylene-*o*-phenylenediarsine (XI), a colourless liquid of b. p. 95°/0·01 mm., and a higher-boiling bromo-derivative, of which supplies were too small for satisfactory identification.

The identity of the tricyclic diarsine (XI) was confirmed by analysis, molecular-weight determinations, and the fact that methyl bromide in the cold gave the monomethobromide and at 100° regenerated the dimethobromide (X). Again, as in case of the diarsines (I) and (III), boiling methyl iodide furnished only the monomethiodide, whereas at 100° the

dimethiodide was formed. Furthermore, this diarsine, like (III), when treated with hydrogen peroxide gave the corresponding diarsine dioxide (XII) which was also characterised as the bishydroxypicrate.

The three ditertiary arsines (I), (III), and (XI) form a series in which both the intensity of odour and the susceptibility to atmospheric oxidation decrease markedly in the above order.

The tricyclic diarsine (XI) is clearly of the same general type as tri-*o*-phenylenediarsine (XIII), prepared by McCleland and Whitworth (*J.*, 1927, 2753; see also Chatt and Mann, *J.*, 1940, 1184). The diarsine (XIII) appeared to differ strikingly from (XI) in one respect, however, because McCleland and Whitworth state that although it forms a dioxide and a tetrabromide, it does not form quaternary salts. This is unexpected, because the fixed disposition of the three valencies of each arsenic atom in (XIII) would appear to be almost ideal for allowing the arsenic atoms to become tetrahedral by valency increase, and the ingress of small groups (such as methyl) by quaternisation should therefore occur as readily as that of oxygen atoms by oxidation: furthermore, whereas quaternisation would thus place no strain on the valencies of the arsenic atoms, the formation of the tetrabromide would involve very considerable strain.



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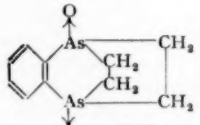

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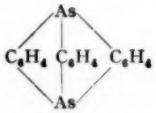

(XIII)

Experiments, in which we have been kindly assisted by Mr. Emrys R. H. Jones, have shown that the diarsine (XIII) is in fact unaffected when heated with an excess of methyl bromide or iodide, even at 100° for 10 hours. When, however, the diarsine was heated with an excess of methyl toluene-*p*-sulphonate at 180° for 4 hours, it was converted into the monomethotoluene-*p*-sulphonate, and no further quaternisation occurred even at 210° during 6·5 hours. [This recalls the behaviour of 5 : 10-dihydro-5 : 10-di-*p*-tolylarsanthren, of which Chatt and Mann (*J.*, 1940, 1184) were able to prepare the monomethiodide but not the dimethiodide.] Since therefore no steric factor strongly influences the quaternisation of the diarsine (XIII), it appears that the combined electronic effect of the three *o*-phenylene groups considerably diminishes the normal reactivity of both tertiary arsine groups, and that, when one has undergone quaternisation, the full positive charge on this arsenic atom (as distinct from the modified positive charge in the arsine oxide) deactivates the second arsine group sufficiently to inhibit further quaternisation.

We are now investigating the reaction of the diarsine (III) with *o*-xylylene dibromide and similar compounds.

Experimental

Quaternary Salts of o-Phenylenebisdimethylarsine (I).—A solution of the arsine (1 g.) in methyl bromide (10 c.c.) was set aside in a sealed tube at room temperature for 12 hours with occasional shaking, crystals rapidly separating. The methyl bromide was allowed to evaporate, and the residue, when recrystallised from acetone containing a small proportion of methanol, gave the *monomethobromide*, m. p. 225—226° (Found: C, 34·9; H, 5·2. $C_{11}H_{19}BrAs_2$ requires C, 34·9; H, 5·2%).

A similar solution of the arsine (1 g.) in methyl bromide (7 c.c.) and methanol (3 c.c.) was heated in a sealed tube at 100° for 3 hours. The excess of solvent was then evaporated, and the heavy residual crystals, when crushed under acetone, collected, and dried in a vacuum, gave the pure *dimethobromide*, m. p. 222—223° with decrepitation at *ca.* 150° (Found: C, 29·8; H, 4·9. $C_{12}H_{22}Br_2As_2$ requires C, 30·3; H, 4·7%).

A solution of the arsine in an excess of methyl iodide was boiled under reflux in a nitrogen atmosphere for 1 hour, salt formation rapidly occurring. The residual crystals, after evaporation of the iodide, were recrystallised from ethanol and furnished the *monomethiodide*, m. p. 228—230° (Found: C, 30·9; H, 4·1. $C_{11}H_{19}IAs_2$ requires C, 30·85; H, 4·4%). The monomethiodide was also readily formed when the original solution was set aside at room temperature.

The previous solution, diluted with methanol, was heated in a sealed tube at 100° for 4 hours. Removal of the solvent gave a slightly hygroscopic crystalline residue which, when washed with methanol and dried at atmospheric pressure, gave the *dimethiodide*, m. p. 222—224° (Found : C, 24·7; H, 4·0. $C_{12}H_{22}I_2As_2$ requires C, 25·2; H, 3·9%).

Thermal Decomposition of the Dibromide (II).—The pure powdered dibromide (65 g.) was placed in a simple distilling-flask fitted with a capillary intake, a water-condenser, and receiver, and evacuated to 0·03 mm. pressure whilst nitrogen was led through the capillary. The dibromide was then heated carefully with the " brush " flame of a Bunsen burner, whereupon decomposition occurred smoothly; the distillate (41 g.), at first quite clear, became ultimately slightly cloudy. To ensure the elimination of traces of unchanged dibromide, the distillate was redistilled without fractionation under similar conditions. The new distillate, when carefully fractionated in nitrogen at 0·5 mm. through a column, gave the fractions : (A) b. p. 80—108°, very small quantity; (B) b. p. 110—130°, 10·6 g., colourless; (C) b. p. 130—140° (mainly at 136—138°), 22·9 g., very faintly golden; (D) a small semisolid residue. No sharp distinction between fractions (B) and (C) could be obtained.

Fraction (B) was twice refractionated, and 1 : 4-*dimethylethylene-o-phenylenediarsine* (III) ultimately obtained as a colourless liquid of moderate odour, b. p. 94—97°/0·015 mm. (Found : C, 42·0; H, 5·2%; *M*, ebullioscopic in 1·235% ethanol solution, 289. $C_{10}H_{14}As_2$ requires C, 42·3; H, 5·0%; *M*, 284).

Fraction (C), even after four refractionations, gave impure 1-bromo-4-methylethylene-*o*-phenylenediarsine (IV), b. p. 120°/0·3 mm. (Found : C, 32·3; H, 3·8. $C_9H_{11}BrAs_2$ requires C, 30·95; H, 3·2%).

In later experiments, when only the diarsine (III) was required, the crude distillate was added slowly with stirring to an excess of methylmagnesium iodide in ether under nitrogen. The ethereal product, when hydrolysed with aqueous ammonium chloride and worked up in the usual way, furnished on one distillation the pure diarsine (III), b. p. 106—108°/0·3 mm. (Found : C, 42·6; H, 5·3%), giving the same crystalline derivatives as the above sample.

When the thermal decomposition of the dibromide (II) was carried out by heating the dibromide either slowly in a metal-bath at a high vacuum, or in a vigorous stream of nitrogen at atmospheric pressure, various other products of uncertain constitution were obtained.

1 : 4-*Dimethylethylene-o-phenylenediarsine* (III).—This diarsine gave the following derivatives, the quaternary salts being prepared under the same conditions as those of the diarsine (I) : *Monomethobromide*, very soluble in methanol but separating readily from ethanol as colourless crystals, m. p. 228° (effervescence) (Found : C, 35·0; H, 4·5. $C_{11}H_{17}BrAs_2$ requires C, 34·85; H, 4·5%). Dimethobromide, prepared to check the identity of (III), and forming colourless crystals, m. p. 254° (effervescence), unchanged by admixture with the original dibromide. *Monomethiodide*, m. p. 250° (effervescence) after recrystallisation from methanol and drying at 100°/0·1 mm. (Found : C, 31·45; H, 4·15. $C_{11}H_{17}IAs_2$ requires C, 31·0; H, 4·0%). *Dimethiodide*, m. p. 245—246°, when recrystallised from methanol and dried at 75°/0·1 mm. for 2 hours (Found : C, 24·95; H, 3·7. $C_{12}H_{20}I_2As_2$ requires C, 25·4; H, 3·55%).

Dioxide (V).—A mixture of the diarsine (III) and an excess of aqueous hydrogen peroxide (" 20-vol.") was diluted with sufficient acetone to give a clear solution, which was kept at 35° for 4 hours, then concentrated on a water-bath, and finally evaporated in a vacuum to a sticky residue of the dioxide (V). An aqueous solution of the latter, when treated with aqueous picric acid, deposited the *bishydroxypicrate*, yellow crystals, m. p. 179—180°, after recrystallisation from methanol (Found : C, 33·8; H, 2·6; N, 10·9. $C_{22}H_{20}O_{16}N_6As_2$ requires C, 34·1; H, 2·6; N, 10·9%) : it was too soluble in water and ethanol for satisfactory recrystallisation.

*Dibromobis-*1 : 4-*dimethylethylene-o-phenylenediarsine Palladium*.—The arsine, when added to aqueous-ethanolic potassium palladobromide, rapidly deposited a reddish-brown precipitate which became deep orange when the mixture was boiled. The precipitate when recrystallised from methanol gave the above *compound* as deep orange crystals, m. p. 360° (vigorous decomp.) (Found : C, 28·6; H, 3·55; Pd, 12·5. $C_{20}H_{28}Br_2As_4Pd$ requires C, 28·75; H, 3·4; Pd, 12·8%).

1-*Bromo-*4-*methylethylene-o-phenylenediarsine* (IV).—This compound gave the following derivatives. *Monomethobromide* (VII; X = Br). (*a*) A solution of (IV) in an excess of methyl bromide in a sealed tube was set aside at room temperature for 3 days. (*b*) A similar solution, containing in addition some methanol, was heated at 100° for 5 hours. In both cases, evaporation of the solvent gave the *monomethobromide*, m. p. 240° (effervescence) after recrystallisation from methanol (Found: C, 27·2; H, 3·5. $C_{10}H_{14}Br_2As_2$ requires C, 27·0; H, 3·2%). 1-*Iodo-*4-*methylethylene-o-phenylenediarsine monomethiodide* (VII; X = I) readily separated when a solution of (IV) in methyl iodide was boiled under reflux, and on recrystallisation from methanol

formed deep yellow crystals, m. p. 199—200° (Found : C, 22·5; H, 2·7. $C_{10}H_{14}I_2As_2$ requires C, 22·3; H, 2·6%). 4-*Methyl*-1-(*N*-*pentamethylenethiocarbamylthio*)*ethylene*-o-*phenylenediarsine* (VIII) readily separated when ethanolic solutions of the bromo-arsine (IV) and of piperidine *N*-pentamethylenedithiocarbamate were mixed and warmed : it formed cream-coloured crystals, m. p. 101—101·5°, from ethanol (Found: C, 41·6; H, 5·1; N, 3·2%; *M*, ebullioscopic in 1·08% ethanolic solution, 433. $C_{15}H_{21}NS_2As_2$ requires C, 41·9; H, 4·9; N, 3·3%; *M*, 429·3).

The bromo-arsine (IV) was also added to an excess of ethereal methylmagnesium iodide, and thus converted into the diarsine (III), which was identified by analysis and by conversion into the dimethobromide and dimethiodide previously described.

Diethylene-o-*phenylenediarsine Dimethobromide* (X).—A mixture of the diarsine (III) (11·6 g.) and pure ethylene dibromide (3·5 c.c., 1 mol.) was heated in an oil-bath under reflux in nitrogen at 120—125° for 3 hours. Solidification rapidly started and after *ca.* 2 hours' heating was complete. The cold pulverised material, when recrystallised from methanol, gave the hygroscopic *dimethobromide*, m. p. 240° (effervescence) (Found : C, 30·15; H, 4·0. $C_{12}H_{18}Br_2As_2$ requires C, 30·5; H, 3·8%). Cold aqueous solutions of this salt and of sodium picrate when mixed deposited the *dimethopicrate*, pale yellow needles, m. p. 230° after recrystallisation from water (Found : C, 37·6; H, 3·2; N, 10·6. $C_{24}H_{22}O_{14}N_6As_2$ requires C, 37·5; H, 2·9; N, 10·9%). *X*-Ray powder photographs gave independent evidence that this picrate was structurally distinct from, although similar to, that obtained from (II).

The diarsine (III) combined similarly with trimethylene dibromide, but the hard glassy product could not be satisfactorily recrystallised.

Thermal decomposition of the dibromide (X). The pure dry dibromide (12·8 g.) was heated at 270°/0·5 mm. whilst a fine stream of nitrogen was passed through a capillary tube into the distilling flask. Decomposition occurred smoothly with the formation of a colourless distillate, no residue ultimately remaining. The distillate was redistilled without fractionation, and then carefully refractionated in nitrogen through a short column. Two fractions were obtained at 0·065 mm. : (A) b. p. 120—125°, 3·4 g.; and (B) b. p. 130—135°, 2·3 g.; the separation of the two fractions was apparently distinct.

Fraction (A) on refractionation gave *diethylene*-o-*phenylenediarsine* (XI) as a slightly hygroscopic colourless liquid, b. p. 95—96°/0·01 mm. (Found : C, 42·7; H, 4·6%; *M*, cryoscopic in 0·857% benzene solution, 274. $C_{10}H_{12}As_2$ requires C, 42·6; H, 4·3%; *M*, 282). It had an odour fainter than that of (III).

Fraction (B) on refractionation ultimately gave a liquid, b. p. 105—107°/0·014 mm., which was apparently still a mixture (Found : C, 34·6; H, 3·8; Br, 16·1%).

Derivatives of Diethylene-o-*phenylenediarsine* (XI).—The *monomethobromide* was prepared as before at room temperature, and after recrystallisation from ethanol had m. p. 244° (effervescence) (Found : C, 34·9; H, 4·1. $C_{11}H_{15}BrAs_2$ requires C, 35·0; H, 4·0%). The use of an excess of methanolic methyl bromide at 100° regenerated the dimethobromide (X), which, after recrystallisation from ethanol and drying at 100°/0·1 mm. for 6 hours, had m. p. 239—240° (effervescence), unchanged by admixture with the earlier sample (Found : C, 30·2; H, 4·1%). A solution of (XI) in methyl iodide, when boiled under reflux, gave the *monomethiodide*, which after recrystallisation from methanol had m. p. 240° (effervescence, the crystals showing considerable agitation from 210°) (Found : C, 31·5; H, 4·15. $C_{11}H_{15}IAs_2$ requires C, 31·2; H, 3·6%). A similar solution, when heated at 100° for 4 hours, gave the *dimethiodide*, which, recrystallised from methanol and then dried at 60°/0·1 mm. for 4 hours, had m. p. 260° (effervescence) (Found : C, 25·4; H, 3·4. $C_{12}H_{18}I_2As_2$ requires C, 25·5; H, 3·2%). The two diquaternary salts are thus, like those of (III) but unlike those of (I), stable to moderate heat.

A suspension of the diarsine (XI) in cold hydrogen peroxide (" 20-vol.") was set aside overnight, and the clear solution thus obtained was gently evaporated. The residue of the crude dioxide (XII) became sticky on exposure to air : its aqueous solution was therefore treated with aqueous picric acid, the *bishydroxypicrate* being precipitated as yellow crystals, m. p. 184° after recrystallisation from water (Found : C, 34·5; H, 2·5; N, 11·1. $C_{22}H_{18}O_{16}N_6As_2$ requires C, 34·2; H, 2·3; N, 10·9%).

Attempted Quaternisation of Tri-o-*phenylenediarsine* (XIII).—(1) A mixture of the diarsine (0·5 g.), methyl bromide (1 c.c., *ca.* 9 mols.) or methyl iodide (0·6 c.c., *ca.* 14 mols.), and methanol (1 c.c.) was heated in a sealed tube in nitrogen at 100° for 10 hours, and then evaporated to dryness. The residue, when recrystallised from much ethanol, gave the unchanged diarsine (XIII), m. p. 286—287°, unchanged by admixture with the original sample, of m. p. 285—286°. Almost the whole of the original diarsine was thus recovered.

(2) A mixture of the powdered diarsine (0·2 g.) and methyl toluene-*p*-sulphonate (0·6 g., 6 mols.) was heated at 180° for 4 hours, complete solution being obtained at *ca.* 160°. The cold viscous residue when stirred with ether deposited the *monomethotoluene*-p-*sulphonate* as a white powder, very soluble in cold ethanol; recrystallisation from water gave the very stable *monohydrate*, which after drying at 120°/0·1 mm. for 3 hours had m. p. 238° (Found: C, 53·8; H, 3·8. $C_{26}H_{22}O_3SAs_2,H_2O$ requires C, 53·6; H, 4·1%). Since however the carbon and hydrogen content of the mono- and di-metho-salts are closely similar, an aqueous solution of the pure monohydrate was treated with aqueous sodium picrate, thus precipitating the yellow *monomethopicrate*, which after recrystallisation from methanol and drying at 100°/0·1 mm. for 3 hours had m. p. 226—227° (decomp.) (Found: C, 48·8; H, 3·0; N, 6·6. $C_{25}H_{17}O_7N_3As_2$ requires C, 48·4; H, 2·7; N, 6·75%).

(3) Expt. (2) was repeated, with however 16 mols. of the sulphonate at 210° for 6·5 hours. The product, when purified as before, again gave the monohydrate of the monomethotoluene-*p*-sulphonate, which was not affected by being heated at 140°/0·1 mm. for 15 hours, and again had m. p. 238°, unaffected by admixture with that obtained in Expt. (2). This sample gave the same monomethopicrate, m. p. 226—227° (decomp.), mixed and unmixed.

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797. N-*Substituted Glycosylamines. Part IV.** N-*Aryl*-D-*fructosylamines.*

By C. P. BARRY and JOHN HONEYMAN.

Unsuccessful attempts were made to condense D-fructose with aniline and *p*-toluidine under conditions used for preparing *N*-arylaldosylamines. *N*-Phenyl- and *N*-*p*-tolyl-D-fructosylamines have been prepared by boiling the amine and fructose in anhydrous ethanol in the presence of the amine hydrochloride. These products were acetylated and benzoylated to crystalline esters which were hydrolysed to D-fructose 1 : 3 : 4 : 5-tetra-acetate and 1 : 3 : 4 : 5-tetrabenzoate. The same *N*-phenylfructosylamine tetra-acetate has been prepared from aniline and fructopyranosyl chloride tetra-acetate. Thus, these *N*-aryl-D-fructosylamines react as pyranose compounds.

IN contrast with the large number of *N*-arylaldosylamines which have been reported, only four *N*-arylketosylamines are known. Sorokin (*Ber.*, 1886, **19**, 513; *J. pr. Chem.*, 1888, **37**, 295) condensed aniline and D-fructose in boiling ethanol and obtained in very low yield crystalline *N*-phenyl-D-fructosylamine. Kuhn and Birkofer (*Ber.*, 1938, **71**, 621) found that for *p*-phenetidine to react with D-fructose or L-sorbose in alcohol ammonium chloride is required as catalyst. The *N*-*p*-ethoxyphenylketosylamines, isolated in 15% yield, were crystalline solids melting with decomposition. Since our work was carried out an abstract (*Chem. Abs.*, 1951, **45**, 9481) has appeared in which *N*-*p*-tolyl-D-fructosylamine is mentioned, but no details are given of its preparation: the original paper (Inoue and Onodera, *J. Agric. Chem. Soc., Japan*, 1948, **22**, 70) is not yet available to us. No esters or ethers of *N*-substituted ketosylamines have previously been recorded; indeed, Irvine and McNicoll (*J.*, 1910, **97**, 1450) report their failure to make aniline derivatives of methyl fructoses.

The less ready reaction of fructose with amines has been used by Weygand, Perkow, and Kuhner (*Ber.*, 1951, **84**, 594) to obtain crystalline fructose from invert sugar by precipitating the glucose as *N*-*p*-nitrophenyl-D-glucosylamine. We have confirmed the failure of aniline and *p*-toluidine to react with fructose under conditions usually successful for aldoses. At room temperature in aqueous alcohol, as described for aldoses by Ellis and Honeyman (*J.*, 1952, 1490), and in hot aqueous suspension (Weygand, *Ber.*, 1939, **72**, 1663) no condensation occurred. Unchanged fructose was recovered when the compounds were heated in boiling absolute alcohol, but the addition of ammonium chloride or, better, aniline hydrochloride catalysed the reaction and a small proportion of crystalline *N*-phenyl-D-fructosylamine was isolated as well as unchanged fructose. Increasing the

* Part III, Ellis and Honeyman, *J.*, 1952, 2053.

reaction time beyond an hour did not increase the yield of product, but decreased the amount of recovered fructose. The amount of condensation was increased by removing water during the reaction, but the method which gave the best yield involved anhydrous ethanol as solvent. With this, the optimum time was seven minutes at boiling point: longer heating did not lead to more product but increased the discoloration. These results taken together suggest the possibility of this being an equilibrium reaction and, therefore, differing from the aldose condensations. The same method has been used successfully to prepare crystalline *N*-*p*-tolyl-D-fructosylamine. No anomers have been obtained, although the compounds mutarotated in alcohol and in pyridine. The melting points of these compounds are really decomposition temperatures, of little value as a criterion of purity or for correlating the compounds with those obtained by Sorokin (*loc. cit.*) and Inoue and Onodera (*loc. cit.*). Comparison of the specific rotations is possible in the case of *N*-phenyl-D-fructosylamine only and indicates that our compound is the same as Sorokin's. Judgment is suspended in the case of the other compound until further information is available for Inoue and Onodera's *N*-*p*-tolyl-D-fructosylamine. Although they found that their compound is more readily hydrolysed by acid than a number of *N*-*p*-tolylaldosylamines, we found that both our compounds have excellent storage properties. Some samples have now been kept under ordinary laboratory conditions for over two years without deterioration, whereas arylaldosylamines decompose completely in a few months. *N*-Phenyl- and *N*-*p*-tolyl-D-fructosylamine have been acetylated and benzoylated by the method described by Ellis and Honeyman (*J.*, 1952, 2053), to give crystalline tetra-acetates and tetrabenzoates. The ease of hydrolysis of the amine residue in these esters is roughly the same as in the corresponding aldose compounds; the greater stability of the benzoates is again marked. The product obtained in this way from the two tetra-acetates was D-fructose 1 : 3 : 4 : 5-tetra-acetate, shown to be the same as that obtained by direct acetylation of fructose by Pacsu and Rich's process (*J. Amer. Chem. Soc.*, 1933, **55**, 3018). Similarly the two tetrabenzoates were converted into D-fructose 1 : 3 : 4 : 5-tetrabenzoate, identical with a specimen prepared by the direct benzoylation of fructose by Brigl and Schirle's method (*Ber.*, 1933, **66**, 325). This proves that the four *N*-aryl-D-fructosylamine esters which we have prepared have pyranose ring structures and that their acetyl or benzoyl groups are linked to oxygen. Confirmation of this was obtained by isolating the same *N*-phenyl-D-fructopyranosylamine tetra-acetate on condensing aniline with D-fructopyranosyl chloride tetra-acetate. In contrast with the aldose series, however, D-fructose 1 : 3 : 4 : 5-tetra-acetate was recovered after 30 minutes' boiling with aniline in anhydrous ethanol containing aniline hydrochloride as catalyst. Longer reaction resulted in much decomposition. Under similar conditions, no condensation took place between aniline and D-fructose 1 : 3 : 4 : 5-tetrabenzoate, 1 : 3 : 4 : 6-tetrabenzoate, or 1 : 3 : 4 : 5 : 6-pentabenzoate. The non-reactivity of the 1 : 3 : 4 : 6-tetrabenzoate was further indicated by the isolation of benzanilide. Attempts to obtain crystalline products by treating aniline with D-fructose 1 : 3 : 4 : 6-tetra-acetate and with D-fructofuranosyl bromide tetrabenzoate were unsuccessful. Methylation of *N*-phenyl-D-fructosylamine by Honeyman and Ellis's method (*loc. cit.*, p. 2053) led to extensive decomposition.

Experimental

Ethanol is used throughout to signify ordinary absolute alcohol. Anhydrous ethanol was prepared by drying ethanol with ethyl phthalate and sodium.

Volatile solvents were evaporated under reduced pressure. All initial values for $[\alpha]_D$ were obtained where necessary by extrapolation to zero time.

Attempted Reaction of Aniline with Fructose.—Fructose was recovered from the attempted condensation of fructose and aniline in boiling water (30 minutes) and in boiling ethanol (2 hours). Longer reaction times led to excessive decomposition.

Reaction of Aniline with Fructose, with Ammonium Chloride as Catalyst.—A solution of aniline (1·4 ml.), fructose (2 g.), and ammonium chloride (0·04 g.) in ethanol (8 ml.) was boiled under reflux for 1 hour. Ether (20 ml.) was then added, precipitating a dark syrup, from which fructose (60%) crystallised on trituration with alcohol. Addition of more ether (20 ml.) to the reaction solution precipitated a solid which, after recrystallisation from ethanol, formed colourless plates (0·3 g., 10%) of *N*-phenyl-D-fructosylamine, m. p. 150° (decomp.).

Preparation of N-*Phenyl*-D-*fructosylamine*.—(*a*) A solution of aniline (2·8 ml.), fructose (4 g.) and ammonium chloride (0·1 g.) in ethanol (16 ml.) and benzene (8 ml.) was boiled under reflux for 1½ hours, the condensate being returned to the reaction vessel through a column of quicklime. The dark solution, left at 0° for several days, deposited a solid which, after being washed with ether and recrystallised from ethanol, was *N*-phenyl-D-fructosylamine (1·7 g., 30%) m. p. 150°, $[\alpha]_D^{19}$ −203·6° ⟶ −161·0° (*c*, 0·2 in ethanol).

Fructose (1·6 g., 40%) was obtained by adding ether to the reaction mother-liquor.

(*b*) The same result was obtained when (*a*) was modified by using aniline hydrochloride (0·2 g.) instead of ammonium chloride and a time of 15 minutes.

(*c*) Aniline (1·5 ml.) was boiled for 15 minutes with fructose (2 g.) and aniline hydrochloride (0·1 g.) in ethanol (10 ml.) and benzene (5 ml.). A mixture of ethanol and benzene (1 : 1) was run in at the same rate as liquid distilled. The same product (35%) was purified as in (*a*).

(*d*) A solution of aniline (1·4 ml.), fructose (2 g.), and aniline hydrochloride (0·1 g.) in anhydrous ethanol (7 ml.) was boiled under reflux for 7 minutes. After being kept at 0° overnight, the crystalline precipitate (2 g.) was purified as before, and found to be *N*-phenyl-D-fructosylamine (1·35 g., 70%, calc. on fructose not recovered), m. p. 149° (decomp.), $[\alpha]_D^{17-19}$ −209·3° ⟶ −203·8° (*c*, 0·2 in ethanol), $[\alpha]_D^{19}$ −209·4° ⟶ −164·1° (*c*, 1·0 in pyridine), $[\alpha]_D$ −220·6° ⟶ −202·5° (*c*, 0·6 in 90% ethanol), $[\alpha]_D^{19}$ −206·8° ⟶ −175·6° (*c*, 0·2 in methanol) (Found: C, 56·7; H, 6·9; N, 5·7. Calc. for $C_{12}H_{17}O_5N$: C, 56·5; H, 6·7; N, 5·5%). Sorokin (*loc. cit.*) recorded for this compound m. p. about 147° (decomp.), $[\alpha]_D^{20-23}$ −185·5° (*c*, 1·7 in 90% ethanol), −215·7° (*c*, 0·6 in 90% ethanol), $[\alpha]_D^{20}$ −181·1° (*c*, 1·1 in dry methanol). Mutarotation was not mentioned.

Unchanged fructose (0·4 g.) was isolated from the reaction solution as previously described.

Reaction of p-*Toluidine with* D-*Fructose*.—(*a*) When *p*-toluidine (1·2 g.) was boiled under reflux for 2 hours with fructose (2 g.) and ammonium chloride (0·05 g.) in ethanol (13 ml.) fructose was recovered.

(*b*) Fructose (2 g.) in anhydrous ethanol (10 ml.) was treated with *p*-toluidine (1·5 g.) and *p*-toluidine hydrochloride (0·1 g.) under the conditions in (*d*) above. Recrystallisation of the crude solid from ethanol gave colourless needles (1·4 g., 47%) of N-p-*tolyl*-D-*fructosylamine*, m. p. 138° (decomp.), $[\alpha]_D^{19}$ −207·7° ⟶ −176·9° (*c*, 0·3 in ethanol), $[\alpha]_D^{18}$ −200·4° ⟶ −167·3° (*c*, 1·3 in pyridine) (Found: C, 57·9; H, 7·0; N, 5·5. $C_{13}H_{19}O_5N$ requires C, 58·0; H, 7·1; N, 5·2%). Inoue and Onodera (*loc. cit.*) record for their compound m. p. 154°, $[\alpha]_D$ −168° ⟶ −88° (*c* and solvent not specified).

Acetylation of N-*Phenyl*-D-*fructosylamine*.—A solution of *N*-phenyl-D-fructosylamine (1 g.) in pyridine (5 ml.) and acetic anhydride (5 ml.) was kept at 0° for an hour and overnight at room temperature, and then poured into ice and water and left for an hour. The product, recrystallised from ethanol as colourless crystals (60%), was N-*phenyl*-D-*fructosylamine* 1 : 3 : 4 : 5-*tetra-acetate*, m. p. 151° $[\alpha]_D$ −149·6° (*c*, 1·1 in chloroform) (Found: C, 57·4; H, 5·9; N, 3·1. $C_{20}H_{25}O_9N$ requires C, 56·7; H, 5·9; N, 3·3%).

Hydrolysis of N-*Phenyl*-D-*fructosylamine Tetra-acetate*.—Aqueous formic acid (0·5%; 40 ml.) was added to the tetra-acetate (1 g.) in acetone (30 ml.) and the solution boiled under reflux for 6 hours in nitrogen. The solution was extracted with chloroform, and the extract dried and evaporated. Addition of ether precipitated a solid which, after recrystallisation from ethanol, was identified as β-D-fructose 1 : 3 : 4 : 5-tetra-acetate (60%), m. p. 132°, $[\alpha]_D$ −91·0° (*c*, 0·5 in chloroform), undepressed on admixture with authentic substance prepared directly from fructose. Brauns (*Proc. Roy. Acad. Amsterdam*, 1907—1908, **10**, 563) gives m. p. 131—132°, $[\alpha]_D^{20}$ −91·6° (*c*, 3 in chloroform).

Attempted Condensation of Aniline with D-*Fructose Tetra-acetates*.—Aniline (1·1 ml.) and aniline hydrochloride (0·1 g.) were boiled under reflux for 30 minutes with D-fructose 1 : 3 : 4 : 5-tetra-acetate (2 g.) in anhydrous ethanol (10 ml.). Unchanged tetra-acetate (1·4 g., 70%) was the only compound isolated.

No crystalline product was obtained when aniline (1·1 ml.), aniline hydrochloride (0·1 g.), and D-fructose 1 : 3 : 4 : 6-tetra-acetate (2 g.) were boiled under reflux for from 30 minutes to 5 hours in anhydrous ethanol (10 ml.).

Reaction of D-*Fructosyl Chloride* 1 : 3 : 4 : 5-*Tetra-acetate with Aniline*.—A solution of aniline (1·1 ml.) and D-fructosyl chloride 1 : 3 : 4 : 5-tetra-acetate (2 g.) in dry benzene (20 ml.) was kept at 0° overnight. Aniline hydrochloride was filtered off and the solution evaporated to a syrup. On addition of ethanol, this deposited crystals of *N*-phenyl-D-fructosylamine tetra-acetate (0·22 g., 10%), m. p. 147—148°. After recrystallisation from ethanol the substance had m. p. 151°, undepressed on admixture with the sample prepared as above.

Benzoylation of N-*Phenyl*-D-*fructosylamine*.—Benzoyl chloride (8 ml.) in pyridine (10 ml.) was added at 0° to *N*-phenyl-D-fructosylamine (2·5 g.) in pyridine (10 ml.). After 24 hours at 0°, chloroform (50 ml.) was added and the mixture extracted several times with dilute hydrochloric acid, then dilute sodium carbonate solution, and water. After being dried, the solvent was evaporated, leaving a syrup which crystallised on trituration with ethanol. The product, recrystallised from ethanol as colourless needles (6·2 g., 90%), was N-*phenyl*-D-*fructosylamine* 1 : 3 : 4 : 5-*tetrabenzoate*, m. p. 100—102°, $[\alpha]_D^{20}$ −132·0° (*c*, 0·5 in chloroform) (Found: C, 70·9; H, 5·0; N, 2·4. $C_{40}H_{33}O_9N$ requires C, 71·6; H, 4·9; N, 2·1%).

Hydrolysis of N-*Phenyl*-D-*Fructosylamine Tetrabenzoate*.—(*a*) The tetrabenzoate (1 g.) was recovered after being heated in acetone (25 ml.) for 6 hours in nitrogen with aqueous formic acid (0·5%; 25 ml.).

(*b*) The tetrabenzoate (1 g.) in acetone (25 ml.) was boiled under reflux for 6 hours with concentrated hydrochloric acid (2 ml.) and water (25 ml.). After cooling, water was added and the solution left overnight at room temperature. A solid was deposited, which recrystallised from ethanol as colourless prisms (0·8 g., 90%) of D-fructose 1 : 3 : 4 : 5-tetrabenzoate, m. p. 175—177°, undepressed on admixture with authentic substance, $[\alpha]_D^{19}$ −169·6° ⟶ −165·2° (*c*, 0·67 in chloroform). For this compound Brigl and Schinle (*loc. cit.*) record $[\alpha]_D^{20}$ −164·9° (*c*, 0·4 in chloroform).

Attempted Condensation of Aniline with D-*Fructose Benzoates*.—(*a*) A solution of aniline (40 mg.), aniline hydrochloride (4 mg.), and D-fructose 1 : 3 : 4 : 5-tetrabenzoate (100 mg.) in anhydrous ethanol (0·5 ml.) was boiled under reflux for 6 hours. After addition of light petroleum (b. p. 40—60°) (2 ml.) the solution slowly deposited D-fructose 1 : 3 : 4 : 5-tetrabenzoate (80 mg.), m. p. 169—170°, mixed m. p. 173—174°, $[\alpha]_D^{19}$ −157·2° (*c*, 0·3 in chloroform).

(*b*) Under similar conditions, D-fructose 1 : 3 : 4 : 6-tetrabenzoate was recovered from an attempt to condense it with aniline.

(*c*) Similarly, *keto*-D-fructose 1 : 3 : 4 : 5 : 6-pentabenzoate (75 mg., 75%) was recovered from an attempt to condense it with aniline.

Attempted Condensation of Aniline and D-*Fructofuranosyl Bromide Tetrabenzoate*.—Crude, liquid D-fructofuranosyl bromide tetrabenzoate, prepared as described by Klages and Niemann (*Annalen*, 1937, **529**, 185) from D-fructofuranose 1 : 3 : 4 : 6-tetrabenzoate (5 g.), was dissolved in ether (100 ml.), and aniline (1·7 ml.; 2 eq.) was added. The solution was left overnight, and the deposit of aniline hydrobromide removed. Evaporation of the solvent yielded a dark syrup which could not be purified.

Acetylation of N-p-*Tolyl*-D-*fructosylamine*.—This was achieved by the method used for the *N*-phenyl derivative. The product, recrystallised from ethanol or light petroleum (b. p. 60—80°) as colourless crystals (50%), was N-p-*tolyl*-D-*fructosylamine* 1 : 3 : 4 : 5-*tetra-acetate*, m. p. 129°, $[\alpha]_D$ −141·0° (*c*, 1·5 in chloroform) (Found: C, 57·7; H, 6·1; N, 3·5. $C_{21}H_{27}O_9N$ requires C, 57·7; H, 6·2; N, 3·2%).

Hydrolysis of N-p-*Tolyl*-D-*fructosylamine Tetra-acetate*.—This, carried out as for the *N*-phenyl derivative, gave D-fructose 1 : 3 : 4 : 5-tetra-acetate (*ca.* 50 mg., from 0·2 g.), m. p. 128—130°, mixed m. p. with that prepared from the corresponding *N*-phenyl compound, 131—132°, mixed m. p. with starting substance, 110°.

Benzoylation of N-p-*Tolyl*-D-*fructosylamine*.—Benzoyl chloride (3·2 ml.) in pyridine (4 ml.) was added at −10° to *N*-*p*-tolyl-D-fructosylamine (1 g.) in pyridine (8 ml.). The solution was kept at −10° for ½ hour, then at 0° for 4 hours. The product, isolated in the same way as for the *N*-phenyl derivative, and recrystallised from light petroleum (b. p. 60—80°) and ethylene dichloride as colourless needles (0·8 g., 30%), was N-p-*tolyl*-D-*fructosylamine* 1 : 3 : 4 : 5-*tetrabenzoate*, m. p. 167·5°, $[\alpha]_D^{20}$ −131·4° (*c*, 1·1 in chloroform) (Found: C, 71·7; H, 5·2; N, 1·9. $C_{41}H_{35}O_9N$ requires C, 71·8; H, 5·1; N, 2·0%).

Hydrolysis of N-p-*Tolyl*-D-*fructosylamine Tetrabenzoate*.—When this tetrabenzoate was hydrolysed by the method used for the *N*-phenyl derivative, the product was D-fructose 1 : 3 : 4 : 5-tetrabenzoate (0·16 g., from 0·2 g.), m. p. 173°, mixed m. p. with that prepared from *N*-phenyl-D-fructosylamine, 175°, $[\alpha]_D^{19}$ −163·3° (*c*, 0·5 in chloroform).

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798. *Synthetic Long-chain Aliphatic Compounds. Part X.* 21-Methoxyheneicosanoic Acid † and Some Related Compounds.*

By R. E. Bowman and R. G. Mason.

The compounds mentioned in the title have been prepared by standard methods.

Since the earlier report (Part V; *J.*, 1951, 2748 ‡) of our experiments on methods of ascending the homologous series of saturated fatty acids, we have concentrated our efforts on the preparation of suitable starting materials. Since there appears little likelihood of our completing the work for a considerable time, we report progress to date.

Our preliminary objective was the preparation of 21-methoxyheneicosanoic acid which could be converted into the corresponding bromo-acid. Interaction of very pure methyl 11-bromoundecanoate (I) and sodium methoxide in methanolic solution followed by fractionation furnished methyl 11-methoxyundecanoate (II) in good yield and thence the acid by hydrolysis. The ester (II) was reduced by the Blaise–Bouveault method to 11-methoxyundecanol, converted by phosphorus tribromide into (III). Cason's modification (*J. Amer. Chem. Soc.*, 1946, **68**, 2078) of the Gilman–Nelson ketone synthesis (*Rec. Trav. chim.*, 1946, **55**, 518), as indicated in the scheme, furnished the keto-acid (IV) but in poor yield; a small quantity of 1 : 22-dimethoxydocosane was also isolated, having arisen, presumably, during the preparation of the Grignard reagent. The keto-acid (IV) was readily obtained pure by crystallisation of its potassium salt and was reduced by Huang-Minlon's method (*J. Amer. Chem. Soc.*, 1946, **68**, 2487) to the saturated acid (V).

$$\underset{\text{(I)}}{\text{Br}\cdot[\text{CH}_2]_{10}\cdot\text{CO}_2\text{Me}} \longrightarrow \underset{\text{(II)}}{\text{MeO}\cdot[\text{CH}_2]_{10}\cdot\text{CO}_2\text{Me}} \xrightarrow[\text{(2) PBr}_3]{\text{(1) Redn.;}} \underset{\text{(III)}}{\text{MeO}\cdot[\text{CH}_2]_{11}\cdot\text{Br}}$$

$$\xrightarrow[\text{(2) Cl}\cdot\text{CO}\cdot[\text{CH}_2]_8\cdot\text{CO}_2\text{Et}]{\text{(1) Mg; CdCl}_2} \underset{\text{(IV)}}{\text{MeO}\cdot[\text{CH}_2]_{11}\cdot\text{CO}\cdot[\text{CH}_2]_8\cdot\text{CO}_2\text{H}} \longrightarrow \underset{\text{(V)}}{\text{MeO}\cdot[\text{CH}_2]_{20}\cdot\text{CO}_2\text{H}}$$

By standard methods, the acid (V) has been converted in high yields into 21-bromo- and 21-hydroxy-heneicosanoic acid and 21-methoxyeicosanol. However, overall yields of (V) are low, and other approaches to similar bifunctional compounds will be examined.

Experimental

Unless otherwise specified, light petroleum refers to the grade of b. p. 60—80°.

Methyl 11-Methoxyundecanoate (II).—11-Bromoundecanoic acid was prepared by Ashton and Smith's method (*J.*, 1934, 438) and carefully purified by repeated recrystallisation from light petroleum, to give material of m. p. 50·5—51°. A mixture of the acid (365 g.), methanol (600 ml.), and concentrated sulphuric acid (60 ml.) was refluxed for 4 hours and the cooled mixture poured into water. Methyl 11-bromoundecanoate (366 g.), isolated in the usual manner, distilled as a colourless oil, b. p. 131—132°/5 mm., n_D^{20} 1·4652. The ester (277 g.) was then added during 0·5 hour to a solution of sodium methoxide (1·1 mols.) in dry methanol (350 ml.). After 4 hours' heating under reflux, most of the methanol was removed by distillation and the cooled mixture poured into acidulated water. The product was isolated as usual, and submitted to careful fractionation through a Fenske column (25 cm.) fitted with a reflux head, the course of the fractionation being followed by refractive-index observations. In this manner a total of 203 g. of required ester was obtained, having b. p. 104—105°/0·5 mm., n_D^{20} 1·4375. On hydrolysis the free acid was obtained as a solid, which crystallised from light petroleum at 0° in needles, m. p. 34·5—35·0°, and formed a p-*phenylphenacyl* ester, nacreous leaflets (from aqueous ethanol), m. p. 70° (Found: C, 76·3; H, 8·4. $C_{26}H_{34}O_4$ requires C, 76·1; H, 8·3%). Hunsdiecker (*Ber.*, 1942, **75**, 1190) reported the acid, prepared in the same manner, as having m. p. 32·7° but, since no mention is made of careful fractionation of the product, his material was very likely contaminated with unsaturated acid formed by the elimination reaction.

11-Methoxyundecanol.—The foregoing methyl ester was reduced with sodium and ethanol, as in *Org. Synth.*, Coll. Vol. II, p. 372. By re-esterifying recovered acid and submitting this to

* Part IX, *J.*, 1952, 1057.

† Geneva notation (CO_2H = 1) is used throughout.

‡ Dr. J. H. Gorvin has kindly drawn our attention to a gross error of nomenclature in Part V where the expression -cosanoic acid was used throughout in place of -contanoic acid. Ed.

the same process, an 85% overall yield of the *alcohol*, b. p. 122—124/1 mm., n_D^{20} 1·4473, was obtained (Found: C, 71·2; H, 13·0. $C_{12}H_{26}O_2$ requires C, 71·2; H, 13·0%). In pyridine it gave the 3:5-*dinitrobenzoate*, prisms, m. p. 58° (Found: C, 57·4; H, 6·8. $C_{19}H_{28}O_7N_2$ requires C, 57·6; H, 7·1%).

11-*Methoxyundecyl Bromide* (III).—A mixture of the foregoing alcohol (152 g., 0·75 mol.), redistilled quinoline (33 g., 0·25 mol.), and dry carbon tetrachloride (300 ml.) was cooled to −10° and phosphorus tribromide (70 g., ; 0·26 mol.) added with stirring at such a rate that the temperature did not rise above −5°. The resulting mixture was then boiled under reflux for 1 hour and, after cooling, poured into water. The organic extract was washed successively with dilute hydrochloric acid, dilute aqueous sodium hydroxide, and water, and solvent removed *in vacuo*. The crude residue (150 g.) was then dissolved in light petroleum (b. p. 40—60°; 300 ml.) and extracted with concentrated sulphuric acid (3 × 25 ml.). The acid extracts were quickly diluted with water, whereupon the *methoxy-bromide* separated as an oil. Isolated in the usual manner, it distilled as a colourless oil, b. p. 114—115°/0·25 mm., n_D^{20} 1·4624 (119 g.) (Found: C, 54·8; H, 9·5. $C_{12}H_{25}OBr$ requires C, 54·4; H, 9·4%).

10-*Keto*-21-*methoxyheneicosanoic Acid* (IV).—The preparation of di-(11-methoxyundecyl)-cadmium from the bromide (0·42 mol.) and its reaction with ω-carbethoxynonanoyl chloride were carried out as described by Cason (*Org. Synth.*, 1948, **28**, 75). The total crude reaction product was hydrolysed on the steam-bath for 1 hour with potassium hydroxide (38 g.) in ethanol (750 ml.). The cooled solution deposited impure potassium salts which were filtered off. After being washed with ethanol (150 ml.), they were extracted with boiling acetone (750 ml.) and then ether (750 ml.) and dried. Evaporation of the organic extracts and crystallisation from ethanol furnished 1:22-*dimethoxydocosane* (9 g.) as needles, m. p. 53° (Found: C, 77·6; H, 13·4. $C_{24}H_{50}O_2$ requires C, 77·8; H, 13·6%). The residual potassium salts (108 g.) were then dissolved in acetic acid (300 ml.) and treated at the b. p. with concentrated hydrochloric acid (50 ml.) for 5 minutes. The mixture was poured into water (700 ml.), the product separating (82 g.; m. p. 81—83°). On crystallisation from ethyl acetate (500 ml.; norite) the *keto-acid* (61 g.) separated as plates, m. p. 82·5—83°, unchanged by further crystallisation from acetone or light petroleum (Found: C, 71·4; H, 11·2. $C_{22}H_{42}O_4$ requires C, 71·3; H, 11·4%).

21-*Methoxyheneicosanoic Acid* (V).—The keto-acid was reduced with hydrazine and sodium hydroxide as described for the preparation of *n*-tricosanoic acid (Ames, Bowman, and Mason, *J.*, 1950, 174), to give the *acid*, plates (from acetone), m. p. 74·5—75·0° (Found: C, 74·2; H, 12·4. $C_{22}H_{44}O_3$ requires C, 74·1; H, 12·4%). It formed a *phenacyl* ester, which crystallised from light petroleum (norite) in plates, m. p. 68·5—69·0° (Found: C, 75·8; H, 10·5. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

21-*Bromoheneicosanoic Acid*.—A mixture of the foregoing acid (2 g.), hydrogen bromide in acetic acid (12 ml. of 50%), and concentrated sulphuric acid (4 ml.) was heated at 100° over 4 hours. The cooled mixture was poured into water, and the resulting solid (m. p. 77—79°) re-treated in a similar manner for 6 hours at 100°. The crude product then had m. p. 78—81° and furnished on crystallisation from light petroleum (norite) the *bromo-acid* (1·8 g.) as leaflets, m. p. 82·5—83° (Found: C, 62·3; H, 10·1. $C_{21}H_{41}O_2Br$ requires C, 62·2; H, 10·1%).

21-*Hydroxyheneicosanoic Acid*.—The corresponding bromo-acid (1 g.) was heated under reflux with a solution of potassium acetate (3 g.) in acetic acid (15 ml.) for 4 hours and the solution poured into water. The solid was collected by filtration and treated with N-sodium hydroxide (50 ml.) and pure dioxan (40 ml.) for 2 hours at the b. p. 20N-Sulphuric acid (6 ml.) was added and, after 3 minutes' refluxing, the mixture was poured into water, and the solid product filtered off. Crystallisation from acetone furnished the *hydroxy-acid* as laths, m. p. 99·5—100° (Found: C, 73·8; H, 12·2. $C_{21}H_{42}O_3$ requires C, 73·6; H, 12·4%).

21-*Methoxyheneicosanol*.—21-Methoxyheneicosanoic acid (2 g.) was added to lithium aluminium hydride (1·5 g.) in ether (30 ml.) containing toluene (15 ml.), and the mass heated under reflux for 12 hours. The cooled mixture was treated with ethanol and then dilute hydrochloric acid. The organic extract was washed successively with dilute hydrochloric acid, dilute sodium hydroxide solution, and water, and dried ($CaSO_4$). Evaporation furnished the crude *alcohol* which crystallised from light petroleum, and then acetone, in rhombohedra (1·7 g.), m. p. 69—69·5° (Found: C, 77·1; H, 13·2. $C_{22}H_{46}O_2$ requires C, 77·1; H, 13·5%).

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799. *The Characteristic Infra-red Absorption Frequencies of Aromatic Nitro-compounds.*

By R. R. Randle and D. H. Whiffen.

The characteristic infra-red absorption frequencies of aromatic nitro-groups in 23 compounds in the range 700—1800 cm.$^{-1}$ are considered and the average values shown to be : 1518 cm.$^{-1}$ for the antisymmetrical N–O stretching, 1349 cm.$^{-1}$ for the symmetrical N–O stretching, and 849 cm.$^{-1}$ for the C–N stretching vibrations.

A number of nitrobenzene and nitrodiphenyl derivatives have been examined as part of a programme on the investigation of the characteristic infra-red absorption frequencies of benzene derivatives. Before conclusions can safely be drawn about the benzene ring frequencies, it is necessary to recognize and discount characteristic frequencies of the aromatic nitro-group, and evidence on this topic is presented here.

The standard tables of characteristic frequencies (Thompson, *J.*, 1948, 328; Williams, *Rev. Sci. Instr.*, 1948, **19**, 135) indicate infra-red absorption by nitro-groups in general in the ranges 1550—1600 and 1300—1350 cm.$^{-1}$. The nitronaphthalenes measured by Hathway and Flett (*Trans. Faraday Soc.*, 1949, **45**, 818) all show strong bands near 1345 cm.$^{-1}$ and the existence of the two frequencies is confirmed by studies of Raman spectra (see Landolt–Börnstein, "Tabellen," 1 Band, Atom- und Molekular-Physik, 2 Teil, Molekeln 1, Table 14145, XVII). These two characteristic frequencies are amply confirmed for aromatic compounds by the present work and seem to be strongly active in infra-red absorption. In view of the complete assignment of some simple nitroparaffins by Smith, Pan, and Nielsen (*J. Chem. Phys.*, 1950, **18**, 706) the frequency at 1518 cm.$^{-1}$ must be assigned to the antisymmetrical and that at 1349 cm.$^{-1}$ to the symmetrical valency stretching mode of the nitro-group. Smith, Pan, and Nielsen also place the C–N stretching frequencies in the region 800—900 cm.$^{-1}$. For the aromatic nitro-compounds there does seem to be a strong band at the centre of this range, and the table shows its exact position for each of the 23 compounds whose spectra have been measured; the table also shows the positions of the strong bands near 1518 cm.$^{-1}$ and 1349 cm.$^{-1}$. In a few cases alternative bands are possible for the correlation and these are given in parentheses; in some cases alternative modes of vibration can be suggested for these frequencies, *e.g.*, the 837-cm.$^{-1}$ absorption of *p*-nitroaniline is probably due to the out-of-plane, umbrella vibration of the hydrogen atoms. Strong bands near 1330 cm.$^{-1}$ due to trifluoromethyl groups (Thompson and Temple, *J.*, 1948, 1432) are omitted from the table. Also given in the table are the mean frequency and standard deviation for each column. The final entries are the mean and standard deviation for the infra-red and Raman frequencies to be found in the literature (Hathway and Flett, *loc. cit.*; Landolt–Börnstein, *op. cit.*; Barnes, Gore, Liddel, and Williams, " Infra-red Spectroscopy," Reinhold, 1944; Randall, Fowler, Fuson, and Dangl, " Infra-red Determination of Organic Structures," van Nostrand, 1949); the numbers in parentheses are the numbers of compounds whose frequencies appear in the mean. For the 849-cm.$^{-1}$ frequency no infra-red figures were found in the literature and only Raman frequencies are included; if two doubtful attributions, *o*-nitrotoluene at 794 cm.$^{-1}$ and *m*-nitrophenol at 817 cm.$^{-1}$, are excluded, the entry would read (8) 862 ± 8, which is a more reasonable standard deviation.

The C–N stretching vibration is surprisingly constant in frequency and approximate intensity, since this mode might have been expected to be susceptible to interaction; 849 cm.$^{-1}$ must, therefore, be considered as a characteristic absorption frequency, and even if it is not by itself a clear indication of an aromatic nitro-group in compounds of unknown structure its presence would provide supporting evidence. It must also be recognized when other features of the spectrum are discussed when aromatic nitro-groups are known to be present, and in particular it must not be confused with the out-of-plane C–H deformation frequency of 1 : 3 : 5-trisubstituted benzenes. In two cases, *o*-nitroaniline at 848

cm.$^{-1}$ and 5-nitro-*o*-toluidine at 1333 cm.$^{-1}$, the absorption is decidedly weak, but there are no cases in the table where the frequencies fail to appear in the infra-red spectra.

Compound	Frequencies, in cm.$^{-1}$ *		
Nitrobenzene	1534 vs	1353 vs	854 *s*
o-Trifluoromethylnitrobenzene	1539 vs	1356 vs	854 s
p- ,, ,,	1530 vs	1360 vs	837 vs
o-Nitroaniline	1513 s	1349 s	848 w
o-Nitroacetanilide	1500 s	1341 s	856 m
m-Nitroaniline	1522 s	1345 s	868 s
m-Nitroacetanilide	(1539 s) 1505 s	1346 s	840 m (824 s)
p-Nitroaniline	1525 s	1348 s	857 s (837 s)
p-Nitroacetanilide	1506 vs	1348 vs	848 vs
5-Nitro-*o*-toluidine (Me = 1)	1515 m	1333 w	827 s
5-Nitro-*o*-acetotoluidide (Me = 1)	(1534 s) 1506 vs	1345 vs	837 m (826 s)
2-Nitro-3-trifluoromethylaniline	1523 s	1351 s	851 m
2-Nitro-3-trifluoromethylacetanilide	1535 vs	1370 vs	850 m
4-Nitro-2-trifluoromethylaniline	1494 s	1341 m	832 m
4-Nitro-2-trifluoromethylacetanilide	1515 vs	1365 vs	850 m
4-Nitro-3-trifluoromethylaniline	1495 vs	1356 s	837 m
4-Nitro-3-trifluoromethylacetanilide	1519 vs	1335 vs	(861 m) 840 s
4-Nitrodiphenyl	1510 vs	1341 vs	854 vs
4-Nitro-3-trifluoromethyldiphenyl	1533 vs	1341 vs	(855 m) 850 s
2-Nitro-3′- ,,	1529 vs	1350 s	855 m
4-Nitro-3′- ,,	1510 s	1347 vs	857 s
4 : 4′-Dinitro-3-trifluoromethyldiphenyl	1529 dbl vs	1348 vvs	852 s 843 s
4 : 4′-Dinitro-3 : 3′-bistrifluoromethyldiphenyl	1529 vs	1348 vs	854 s 843 s
Mean and standard deviation	1518 ± 13	1349 ± 9	849 ± 9
,, ,, literature	(25) 1527 ± 11	(38) 1346 ± 6	(10) 853 ± 26

(No. of compounds in parentheses)

* vs = Very strong, s = strong, m = medium, w = weak, dbl = double.

The compounds whose spectra are available do not form a carefully chosen set which would be required for a discussion of the influences affecting the exact frequencies; but inspection does indicate that factors, such as the existence of *p*-amino-groups or *p*-nitrodiphenyls, which lead to a larger contribution of the form $>C=N\overset{O}{\underset{O}{<}}$ to the electronic structure, lead also to a lowering of the antisymmetrical stretching frequency at 1518 cm.$^{-1}$. When two nitro-groups are present the absorption bands are especially strong and broad, or even double.

Experimental.—The spectra measured were those of the pure liquids or solid films dispersed in a Nujol mull as observed with a Grubb–Parsons spectrometer with a rock-salt prism. The materials were commercial products recrystallized or redistilled, and acetylated where necessary, except for the trifluoromethyl derivatives, which were synthesized by Pettit and Tatlow (*J.*, 1951, 3459).

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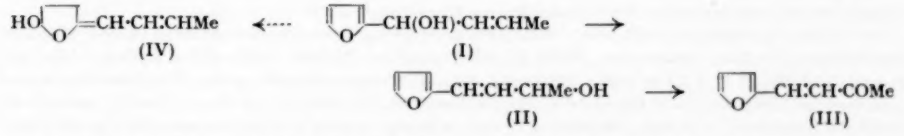
800. *Studies in Molecular Rearrangement. Part IX.* Oxotropic Rearrangements in the Five-membered Heterocyclic Series.*

By E. A. Braude, J. S. Fawcett, and D. D. E. Newman.

The synthesis of the isomeric 1-2′-furyl-3-methylallyl and 3-2′-furyl-1-methylallyl alcohols (I, II) and their thienyl analogues (V, VI), and the acid-catalysed rearrangements of (I) to (II) and of (V) to (VI) are described. 3-2′-Thienyl-1-methylallyl alcohol has been dehydrated to 1-2′-thienylbuta-1 : 3-diene (VII). The light-absorption properties of the various derivatives are recorded and discussed.

In earlier papers (Braude, Jones, and Stern, *J.*, 1946, 396; 1947, 1087; Braude, Fawcett, and Newman, *J.*, 1950, 793) oxotropic rearrangements of a series of 1-arylallyl alcohols have been described. It was demonstrated that aryl groups have a strong activating influence and cause almost complete displacement of the equilibrium to one side, owing to the resonance stabilisation associated with the conjugated 3-arylallyl systems. It was of interest to extend this work to some heterocyclic derivatives, in order to demonstrate the conjugating properties of the heterocyclic groups and, more particularly, for quantitative study of the effects of such groups on reactivity (cf. following paper). This paper describes the synthesis and rearrangement of 1-2′-furyl- and 1-2′-thienyl-3-methylallyl alcohol. Attempts to obtain the corresponding 2′-pyrryl derivative have, so far, been unsuccessful.

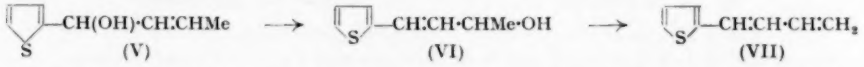
The alcohol (I) was readily obtained from 2-furylmagnesium iodide and crotonaldehyde. On treatment with dilute mineral acid, it underwent rearrangement in the expected manner to the isomer (II), which was also prepared from β-2-furylacraldehyde and methylmagnesium bromide and was characterised as the *p*-nitrobenzoate. The constitution of (II) was further confirmed by oxidation with acetone and aluminium *tert.*-butoxide to furfurylideneacetone (III), characterised as the 2 : 4-dinitrophenylhydrazone. Comparison of the ultraviolet light absorption properties of (II) and of the rearrangement product of (I) showed that the isomerisation is over 98% complete. An alternative mode of rearrangement, involving migration of the hydroxyl group into the ring to give (IV), can be envisaged, corresponding to that observed in the case of 2-furyldiphenylmethanol and similar derivatives (Ushakov and Kutcharov, *J. Gen. Chem. Russia*, 1944, **14**, 1073, 1080, 1087; 1950, **20**, 1885; cf. Braude, *Quart. Reviews*, 1950, **4**, 423), where migration in the side chains is not possible. No trace of (IV) was detected, however, under the conditions employed and this is not surprising since the propenyl group will be more susceptible than the furan ring to nucleophilic attack by a water molecule which constitutes the rate-determining step of the reaction (Braude, *loc. cit.*). Moreover, if any of the isomer (IV) were formed, the ensuing equilibrium between (IV) and (II) would be expected to lie far on the side of (II) which possesses a considerably higher degree of resonance stabilisation derived from the intact furyl system.



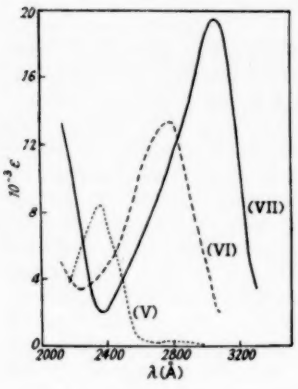
The alcohol (V) was similarly obtained from crotonaldehyde and 2-thienylmagnesium iodide, or, more conveniently, 2-thienylsodium (Schick and Hartough, *J. Amer. Chem. Soc.*, 1948, **70**, 287). Rearrangement under the influence of dilute hydrochloric acid gave exclusively the isomer (VI), which was also prepared from β-2-thienylacraldehyde and methylmagnesium bromide and characterised as the *p*-nitrobenzoate. As with the furyl analogue, spectral measurements showed that the isomerisation of (V) to (VI) is quantitative. Dehydration of (VI) with potassium hydrogen sulphate under very carefully con-

* Part VIII, *J.*, 1951, 2093.

trolled conditions afforded the highly unstable thienylbutadiene (VII). Attempts to prepare this diene by the dehydration of other 2-thienylbutenols have since been described by Gmitter and Benton (*J. Amer. Chem. Soc.*, 1950, **72**, 4586) who were only able to isolate it in the form of Diels–Alder adducts.



Ultra-violet light absorption data for the main derivatives described and for the phenyl analogues are collected in the Table. The alcohols (I) and (V) show bands near 2200 and 2400 Å respectively, which are due to the unconjugated furyl and thienyl groups and may be compared with the " E "-band near 2100 Å associated with a monoalkylated phenyl group (cf. *Ann. Reports*, 1945, **42**, 108; Bowden and Braude, *J.*, 1952, 1068). The isomers (II) and (VI) exhibit new bands at longer wave-lengths which are due to the conjugated vinylfuran and vinylthiophen systems (cf. Laitinen, Miller, and Parks, *J. Amer. Chem. Soc.*, 1947, **69**, 2707; Kuhn and Dann, *Annalen*, 1941, **547**, 293; Jackman, Bolen, Nachod, Tullar, and Archer, *J. Amer. Chem. Soc.*, 1949, **71**, 2301) and may be compared with the band near 2500 Å associated with a styryl group. Lastly, the thienylbutadiene (VII) exhibits highly characteristic absorption at still longer wave-lengths which may be compared with that of phenylbutadiene (see Table and Fig.). It is noteworthy that the wave-length displacements of the bands of the conjugated with respect to the unconjugated derivatives are of the same order in the phenyl and the heterocyclic derivatives; this indicates that what may loosely be called the " extent of conjugation " with an ethylenic bond is similar for the phenyl, furyl, and thienyl groups.



Ultra-violet light absorption data (Å) *(ethanol solutions).*

	X·CH(OH)·CH:CHMe		X·CH:CH·CHMe·OH			X·CH:CH·CH:CH₂		
	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	Δλ †	$\gamma_{max.}$	ε	Δλ †
X = Phenyl [1]	2100	10,000	2510	19,500	410	2800	28,000	700
X = 2-Furyl *	2200	10,200	2650	18,000	350	—	—	—
X = 2-Thienyl	2360	10,000	2800	13,500	440	3070	22,000	690

* Main bands only (cf. Experimental section).
† Shifts with respect to first column.
[1] Braude, Jones, and Stern, *J.*, 1947, 1087.

Experimental

M. p.s are uncorrected. Light-absorption data were determined on a Hilger Spekker instrument and refer to ethanol solutions unless otherwise stated.

1-2′-*Furyl*-3-*methylallyl Alcohol*.—Ethyl bromide (0·5 g.) and then 2-iodofuran (47 g.; Gilman and Wright, *J. Amer. Chem. Soc.*, 1933, **55**, 3307) in ether (100 ml.) were added during 1 hour to magnesium filings (7·5 g.) in ether (500 ml.), with stirring under nitrogen. The resulting solution was decanted and to it freshly distilled crotonaldehyde (14·5 g.) in ether (50 ml.) was added during 1 hour at 0°. After a further 2 hours' stirring, excess of aqueous ammonium chloride was added and the ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated from a trace of potassium carbonate, to give the *alcohol* (12 g., 36%), b. p. 48—50°/0·02 mm., n_D^{23} 1·5018 (Found: C, 69·3; H, 7·1. $C_8H_{10}O_2$ requires C, 69·7; H, 7·3%). Light-absorption: $\lambda_{max.}$ 2200, 2690, 2780, and 2890 Å; ε 10,200, 1200, 1100, and 900, respectively.

3-2′-*Furyl*-1-*methylallyl Alcohol*.—(*a*) β-2-Furylacraldehyde (52 g.; Kornig and Hey, *Ber.*, 1925, **58**, 2559) in ether (300 ml.) was added dropwise to a stirred solution of methylmagnesium bromide (from magnesium, 10 g., and methyl bromide, 42 g.) in ether (500 ml.) at −10°. After 2 hours, excess of aqueous ammonium chloride was added and the products were worked up as above, giving the *alcohol* (32 g., 55%), b. p. 58°/0·02 mm., n_D^{18} 1·5291 (Found: C, 69·6; H, 7·4.

$C_8H_{10}O_2$ requires C, 69·7; H, 7·3%). Light absorption: $\lambda_{max.}$ 2580, 2650, and 2780 Å; ε 17,500 18,000, and 13,000 respectively. The p-*nitrobenzoate* separated from aqueous methanol in crystals, m. p. 59—60° (Found: C, 63·0; H, 4·7; N, 4·9. $C_{15}H_{13}O_5N$ requires C, 62·7; H, 4·5; N, 4·9%). Light absorption: $\lambda_{max.}$ 2660 Å; ε 31,000.

(*b*) 1-2′-Furyl-3-methylallyl alcohol (4 g.) was dissolved in a 0·001M-solution of hydrogen chloride in 60% aqueous dioxan (100 ml.). After 4 hours at room temperature, water was added and the oil which separated was distilled, giving 3-2′-furyl-1-methylallyl alcohol (3 g.), b. p. 52—53°/0·01 mm., n_D^{20} 1·5320, $\lambda_{max.}$ 2580, 2650, and 2760 Å (ε 18,000, 18,500, and 14,000, respectively) which formed a *p*-nitrobenzoate, m. p. 59°, undepressed on admixture with the authentic specimen described above.

2-*Furfurylideneacetone* (4-2′-*Furylbut*-3-*en*-2-*one*).—The above alcohol (4 g.), aluminium *tert.*-butoxide (6 g.), acetone (60 ml.), and benzene (60 ml.) were refluxed for 24 hours. Excess of dilute sulphuric acid was added and the product isolated with ether, giving 2-furfurylideneacetone (2·8 g.) which crystallised from pentane in needles, m. p. 36°, undepressed on admixture with an authentic specimen, b. p. 125°/25 mm., m. p. 37—38°, prepared by the method of Leuck and Cejka (*Org. Synth.*, Coll. Vol. I, 2nd edn., p. 283). It formed a 2 : 4-*dinitrophenylhydrazone* which crystallised from pyridine in crimson rods, m. p. 248° (Found: C, 52·7; H, 4·0; N, 17·7. $C_{14}H_{12}O_5N_4$ requires C, 53·1; H, 3·8; N, 17·7%) ($\lambda_{max.}$ 3130 and 4010 Å; ε 18,000 and 36,500, in chloroform).

3-*Methyl*-1-2′-*thienylallyl Alcohol*.—(*a*) 2-Iodothiophen (40 g.; Minnis, *Org. Synth.*, Coll. Vol. II, p. 357) in ether (150 ml.) was added dropwise to a stirred suspension of magnesium filings (4·8 g.) in ether (50 ml.) at 0° under nitrogen. Reaction was complete after 0·5 hour and crotonaldehyde (13·3 g.) in ether (40 ml.) was then added at 0°. After 2 hours, excess of aqueous ammonium chloride was added and the products were worked up as above, giving the *alcohol* (23·5 g., 80%) as a colourless liquid, b. p. 63—65°/0·2 mm., n_D^{20} 1·5530 (Found: C, 62·6; H, 6·6; S, 20·7. $C_8H_{10}OS$ requires C, 62·35; H, 6·5; S, 20·8%).

(*b*) Bromobenzene (30 g.) in ether (100 ml.) was slowly added to a well-stirred mixture of thiophen (24 g.), finely divided sodium amalgam (from sodium, 9 g., and mercury, 4 g.) and ether (100 ml.) (cf. Schick and Hartough, *J. Amer. Chem. Soc.*, 1948, **70**, 287), and the mixture was then slowly heated to the b. p. and refluxed for 3 hours. After this had cooled, crotonaldehyde (20 g.) in ether (30 ml.) was added dropwise at 5°. After a further hour, ethanol (20 ml.) was carefully added, followed by water (100 ml.). Isolation of the product with ether and fractionation from a trace of potassium carbonate gave the alcohol (28 g., 65%), b. p. 64°/0·1 mm., n_D^{26} 1·5495.

β-2-*Thienylacraldehyde*.—Thiophen-2-aldehyde (25 g.; Dunn, Waugh, and Dittmer, *J. Amer. Chem. Soc.*, 1946, **68**, 2118), freshly distilled acetaldehyde (20 g.), and 2% aqueous sodium hydroxide (200 ml.) were stirred together for 12 hours at room temperature. Isolation of the products with ether and fractionation afforded the *acraldehyde* (17 g., 55%), b. p. 55°/0·05 mm., n_D^{20} >1·68 (Found: C, 60·9; H, 4·5. C_7H_6OS requires C, 60·8; H, 4·4%). Light absorption: $\lambda_{max.}$ 3200 Å; ε 22,500. The *semicarbazone* crystallised from aqueous acetic acid in needles, m. p. 216° (decomp.) (Found: C, 49·0; H, 4·9; N, 21·2. $C_8H_9ON_3S$ requires C, 49·1; H, 4·7; N, 21·5%). Light absorption in dioxan: $\lambda_{max.}$ 3300 Å; ε 37,500. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in dark red plates, m. p. 243° (decomp.) (Found: C, 48·5; H, 3·1; N, 17·2. $C_{13}H_{10}O_4N_4S$ requires C, 49·0; H, 3·2; N, 17·6%). Light absorption in chloroform: $\lambda_{max.}$ 3240 and 4060 Å; ε 13,500 and 39,000.

1-*Methyl*-3-2′-*thienylallyl Alcohol*.—(*a*) The above aldehyde (5·8 g.) in ether (20 ml.) was slowly added to a stirred solution of methylmagnesium bromide (from magnesium, 1 g., and methyl bromide, 4 g.) in ether (100 ml.). After 2 hours, excess of aqueous ammonium chloride was added and the product isolated as above, giving the *alcohol* (4·5 g., 63%), b. p. 72°/0·05 mm., n_D^{17} 1·5898 (Found: C, 62·6; H, 6·5; S, 20·1. $C_8H_{10}OS$ requires C, 62·35; H, 6·5, S, 20·8%). Treatment of the alcohol (0·5 g.) with *p*-nitrobenzoyl chloride (0·7 g.) in dry pyridine gave the p-*nitrobenzoate* which crystallised from aqueous methanol in needles, m. p. 67° (Found: N, 4·8. $C_{15}H_{13}O_4NS$ requires N, 4·6%). Light absorption: λ_{max} 2650 and 2810 Å; ε 26,000 and 22,000.

(*b*) 3-Methyl-1-2′-thienylallyl alcohol (3 g.) was dissolved in a 0·1M-solution of hydrogen chloride in 60% aqueous acetone (150 ml.). After 24 hours at room temperature, water (500 ml.) was added and the product isolated with ether. Fractionation from a trace of potassium carbonate gave 1-methyl-3-2′-thienylallyl alcohol (1·7 g.), b. p. 80—81°/0·5 mm., n_D^{18} 1·5885, which formed a *p*-nitrobenzoate, m. p. 66°, undepressed on admixture with the authentic specimen described above.

1-2′-*Thienylbuta*-1 : 3-*diene*.—The foregoing alcohol (4 g.) and finely powdered potassium

hydrogen sulphate (0·8 g.) were heated to 70° for 15 minutes *in vacuo* (1 mm.) in a small flask with a wide side-arm fitted with a receiver cooled in solid carbon dioxide. Rapid distillation gave a product (2 g.) which was at once diluted with peroxide-free ether (10 ml.) and dried (K_2CO_3). Fractionation of the ethereal solution gave the *diene* as a colourless liquid, b. p. 73°/0·4 mm., n_D^{22} 1·5977 (Found: C, 70·5; H, 5·8; S, 23·7. C_8H_8S requires C, 70·6; H, 5·9; S, 23·6%).

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SOUTH KENSINGTON, LONDON, S.W.7. [*Received, June 20th*, 1952.]

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801. *The Kinetics of Anionotropic Rearrangement. Part X.* A Comparison of the Effects of the Phenyl, Furyl, and Thienyl Groups on Reactivity.*

By E. A. BRAUDE and J. S. FAWCETT.

The acid-catalysed rearrangements of the substituted allyl alcohols X·CH(OH)·CH:CHMe ⟶ X·CH:CH·CH(OH)Me, where X = 2-furyl and 2-thienyl, in aqueous dioxan have been studied kinetically. The results provide the first quantitative data on the effects of the five-membered heterocyclic systems on side-chain reactivity and are compared with those previously obtained with X = phenyl and *p*-methoxyphenyl. Under identical conditions, the furyl and thienyl derivatives rearrange, respectively, about 40 and 100 times faster than the phenyl analogue and with energies of activation about 3 kcal./mole lower. The mobility of the furyl derivative is very similar to that of the *p*-methoxyphenyl derivative.

The results are discussed in relation to other chemical and physical evidence concerning the electronic influence of oxygen and sulphur atoms.

ALTHOUGH the "aromatic" properties of five-membered heterocyclic compounds, such as furan and thiophen, have been much discussed, there are few quantitative data relating to the reactivity of such systems and their derivatives. In previous papers in this series, it was demonstrated that the acid-catalysed rearrangement of substituted allyl alcohols provides a very suitable basis for quantitative studies of the effects of complex or unstable groups on reactivity and we have now applied this method to a comparison of the influence of the phenyl, furyl, and thienyl groups. As previously, the systems used are the 1-substituted 3-methylallyl alcohols, the syntheses and rearrangements of which have been described in the preceding paper.

Kinetic data for the 2′-furyl and 2′-thienyl derivatives, and for the phenyl and *p*-methoxyphenyl analogues, are summarised in Tables 1 and 2. Under the conditions employed,

TABLE 1. *First-order rate-constants* (10^4k *min.*$^{-1}$) *for the rearrangements* X·CH(OH)·CH:CHMe ⟶ X·CH:CH·CHMe·OH *in aqueous dioxan–0·001*M*-hydrochloric acid* (c_s = *dioxan concentration in vol.* %).

	X = 2-Furyl		X = 2-Thienyl	
	c_s = 60%	80%	60%	80%
0°	99	(35) *	39	(13) *
30	1,660	780	640	290
40	3,990	2,070	1,760	850
50	10,400	5,500	4,950	2380
60	21,000	11,100	10,100	5400

* Solid dioxan tends to crystallise in the medium.

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* Part IX, *J.*, 1950, 800.

TABLE 2. *Relative rate constants (r), Arrhenius energies of activation (kcal./mole) and probability factors* ($k/c_A = Ae^{-E_{Arr.}/RT}$, where c_A = acid concentrations in mole./l).

X	60% Aqueous dioxan			80% Aqueous dioxan		
	r (at 30°)	$E_{Arr.}$	log A	r (at 30°)	$E_{Arr.}$	log A
Phenyl [1]	1	19·5	13·3	1	21·6	14·8
2-Furyl	90	16·2	12·2	114	18·3	13·3
2-Thienyl	35	16·5	12·0	43	19·0	13·5
p-Methoxyphenyl [2]	105	17·9	14·1	—	—	—

[1] *J.*, 1946, 396; 1948, 1982. [2] *J.*, 1947, 1096.

the rearrangements of the heterocyclic derivatives exhibit straightforward first-order kinetics and go to over 98% completion. As observed in other cases (cf. *J.*, 1948, 1982; 1950, 800), the reactions are slower and have higher energies of activation in 80% than in 60% aqueous dioxan. In 60% aqueous dioxan at 30°, the 2-furyl derivative reacts 90 times faster than the phenyl analogue and nearly as fast as the *p*-methoxyphenyl analogue. The 2-thienyl derivative reacts about 35 times faster than the phenyl analogue. [The rate ratios are somewhat dependent on the solvent and are slightly larger in 80% aqueous dioxan, indicating that the solvent effect is in part a primary solvation effect dependent on the substituent, as has been noted previously (*J.*, 1947, 1096).] Table 2 shows that the faster rates of rearrangement of the heterocyclic derivatives compared with the phenyl analogue are due to a lowering of about 3 kcal./mole in the energies of activation, partly offset by a simultaneous decrease in the non-exponential factor of the Arrhenius expression.

DISCUSSION

It is well known that thiophen undergoes electrophilic substitution more readily, and furan still more readily, than benzene, but apart from the present results for the anionotropic rearrangements the only quantitative information concerning the relative reactivities of phenyl, furyl, and thienyl derivatives appears to come from Catlin's data (*Iowa State Coll. J. Sci.*, 1935, **10**, 65) for the dissociation constants of furoic and thenoic acid, and from Kindler's data (*Ber.*, 1936, **69**, 2792) for the alkaline hydrolysis of the corresponding ethyl esters. These are collected in Table 3, together with data for the corresponding *p*-methoxyphenyl and *p*-methylthiophenyl derivatives for comparison. Three facts are immediately apparent. First, the furyl and thienyl groups increase reactivity relatively to phenyl in *all* the reactions (neglecting the slight anomaly of the rather dubious value for ethyl thenoate). Secondly, in anionotropy an oxygen atom attached to a phenyl ring has an accelerating effect very similar to that of a hetero-oxygen atom, but in dissociation and alkaline hydrolysis, oxygen and sulphur atoms attached to a phenyl ring have retarding effects opposite to those of the heterocyclic groups. Thirdly, the effects due to an oxygen atom are always larger than those due to a bivalent sulphur atom, independently of the structural type and of whether the influence is accelerative or decelerative; this is also in agreement with the qualitative evidence concerning direct electrophilic substitution of furan and thiophen.

TABLE 3. *Effects of oxygen- and sulphur-containing substituents.*

X	X·CH(OH)·CH:CHMe [1]	X·CO_2H [2]	X·CO_2Et [3]
Phenyl	1·00	6·3	1·00
2-Furyl	90	75	5·3
2-Thienyl	35	34	(0·9) [4]
p-Methoxyphenyl	105	3·4	0·22
p-Methylthiophenyl-	—	6·1	0·70

[1] Relative rates of acid-catalysed anionotropic rearrangement in 60% aqueous dioxan at 30° (this paper; *J.*, 1947, 1096). [2] Dissociation constants (10^6K) in water (Dippy, *Chem. Reviews*, 1939, **25**, 151; Catlin, *loc. cit.*; Bordwell and Cooper, *J. Amer. Chem. Soc.*, 1952, **74**, 1058). The value for *p*-methylthiobenzoic acid is extrapolated from data for 50% aqueous ethanol. [3] Relative rates of alkaline hydrolysis in aqueous ethanol at 30° (Kindler, *loc. cit.*) or aqueous acetone at 25° (Tommila and Hinshelwood, *J.*, 1938, 1801; Price and Hydock, *J. Amer. Chem. Soc.*, 1952, **74**, 1943). [4] This value appears very doubtful, as the rate constants show >50% drift in the single run quoted.

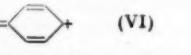
Furyl and thienyl groups may be expected to exert two opposing electronic influences. There will be an electron-withdrawing inductive ($-I$) effect, caused by the electronegativities

of the hetero-atoms; independently of the basis of computation, the values increase in the sequence H< C < S < O (Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, 1940; Coulson, "Valence," Oxford Univ. Press, 1952) and thus $-I_{\text{Phenyl}} < -I_{\text{Thienyl}} < -I_{\text{Furyl}}$. Secondly, there will be an electron-donating mesomeric ($+M$) effect due to the ability of the hetero-atoms to share their unshared p-electron pairs. This mesomeric polarisation can be expressed in terms of contributions from resonance structures such as (I) and (II), which have been estimated by Schomaker and Pauling (*J. Amer. Chem. Soc.*, 1939, **61**, 1769) to be of the order of 15% in furan and 20% in thiophen on the basis of bond-length and dipole-moment data; thus, $\pm M_{\text{Phenyl}} < +M_{\text{Furyl}} \sim M_{\text{Thienyl}}$. Actually the quantitative significance of Schomaker and Pauling's analysis is somewhat uncertain because it neglects the "hybridisation moment" of the hetero-atom (Longuet-Higgins, *Trans. Faraday Soc.*, 1949, **45**, 173); moreover, in the case of thiophen, bond lengths indicate a greater contribution of structures containing S=C bonds than dipole moments. To account for the discrepancy, Schomaker and Pauling postulated some contribution from structures (III) and (IV) of reversed polarity, in which the sulphur valency shell is expanded to a decet of electrons. The participation of the 3*d*-orbitals of sulphur in the hybridisation of the π-electrons of thiophen has been supported by molecular-orbital calculations (Longuet-Higgins, *loc. cit.*) and will decrease the electron-donating properties

(I) (II) (III) (IV)

of the thienyl group; in the terminology of substituent effects, the mesomeric effect of thienyl should be described as $\pm M$, with $+M$ predominating. The additional inductomeric (I') and electromeric (E) effects, representing changes in polarisability which can facilitate the attainment of the transition state in a reaction, will have the same sign as the permanent I and M effects operating in the ground state. Thus, we may have $+E_{\text{Furyl}}$, but $\pm E_{\text{Thienyl}}$ effects.

The influence of the heterocyclic systems may be expected to be paralleled by groups such as methoxyphenyl and methylthiophenyl relative to phenyl. The $-I$ effects will be similar, while the $\pm M$, $\pm E$ effects are represented by contributions from structures such as (V) and (VI). In fact the mesomeric moments of PhOMe and PhSMe calculated

(V)  (VI)

from recorded values (*Trans. Faraday Soc.*, 1934, **30**, Appendix) are approximately 0·07 and 0·13 D and the relation $+M_{\text{O}} \sim +M_{\text{S}}$ is also indicated by the dipole effects of oxygen and sulphur substituents in other unsaturated systems (Hannay and Smyth, *J. Amer. Chem. Soc.*, 1946, **68**, 1005; cf. below).

It is well established that acid-catalysed anionotropy is facilitated by electron-donating substituents, the first step being reversible addition of a proton to the migrating group (cf. Braude, *Quart. Reviews*, 1950, **4**, 404), and the data in Table 3 show that electron-accession increases in the sequence phenyl < thienyl < furyl ~ p-methoxyphenyl. Clearly, in this reaction the combined $+M$ and $+E$ effects outweigh the $-I$ effects and since it has been deduced that $-I_{\text{S}} < -I_{\text{O}}$, and $+M_{\text{O}} \sim +M_{\text{S}}$, it follows that $+E_{\text{S}} < +E_{\text{O}}$, *i.e.*, that the electromeric polarisability of the thienyl group is *less* than that of the furyl and the methoxyphenyl group. The conclusion that $+E_{\text{S}} < +E_{\text{O}}$ is in agreement with Bennett and Hafez's data (*J.*, 1941, 652; cf. Baddeley, *J.*, 1950, 663) on the reaction of p-substituted phenylethyl alcohols R·C_6H_4·CH_2·CH_2·OH with hydrobromic acid; here also the first step is the addition of a proton to the hydroxyl group and the rates increase in the sequence R = H < SMe < OMe. Thus, the sequence of positive electromeric effects due to O and S is the same, whether the atoms are incorporated in a heterocyclic ring or attached to a phenyl group, and equal to the sequence of mesomeric effects. An increase in mesomeric and electromeric interaction with increasing atomic size is expected from polarisability considerations (cf. Ingold, *Chem. Reviews*, 1934, **15**, 225) and from energy consider-

ations of orbital overlap (Mulliken, *J. Amer. Chem. Soc.*, 1950, **72**, 4493); on the other hand, steric considerations of orbital overlap lead to the opposite prediction because the ratio of the electron-shell radius to bond length is less favourable with large atoms (cf. Baddeley, *J.*, 1950, 663). The only other periodic group for which reliable information is available is the halogens; here $+M$ effects decrease with atomic size (Braude and Stern, *J.*, 1947, 1096; Baker and Hopkins, *J.*, 1949, 1089, and earlier references there cited), while the predominant portion of the polarisability effects appears to be inductomeric rather than electromeric (Baker and Hopkins, *loc. cit.*). It is interesting that the relation $+E_S < +E_O$ is the reverse of that predicted by spectral analogies, since the auxochromic properties of SR are much larger than those of OR substituents (Bowden and Braude, *J.*, 1952, 1068).

We now turn to the data for carboxylic acid dissociation and for alkaline hydrolysis of ethyl carboxylic esters. Unlike anionotropy, these reactions are facilitated by electron-withdrawal from the reaction centre but the furyl and thienyl groups again have an activating influence relative to phenyl. This is surprising since the effects of groups usually become reversed in processes of opposite electronic requirements, giving rise, for instance, to an inverse relation between rates of anionotropy and acid dissociation constants (cf. *J.*, 1947, 1096). Moreover, *p*-methoxyphenyl and *p*-methylthiophenyl groups, unlike the heterocyclic groups, do, in fact, have a deactivating influence on the carboxyl reactions in contrast to their influence on anionotropy. In the carboxyl reactions, no $+E$ effects will be brought into play, but $-I$ effects will be reinforced by inductomeric $-I'$ effects and possibly, in the case of sulphur derivatives, by $-E$ effects involving *d*-orbitals. In the case of the OMe and SMe substituents, the data show that the $+M$ effects outweigh even the combined $-I$, $-I'$, and any $-E_S$ effects, thus leading to overall electron accession hindering the reaction, and that $+(-I, +M, -E)_{SMe} < +(-I, +M)_{OMe}$. This is a plausible result in so far as the mesomeric effects will be transmitted more powerfully than the inductive effects across the phenyl ring and will be enhanced by the carboxyl group, while the inductomeric effects are relatively weak (cf. Ingold, *J.*, 1933, 1120); the $-E_S$ effect, if it contributes at all, must evidently be quite weak also.

The unexpected activating influence of the heterocyclic groups on the carboxyl reactions are less easily explained. The data indicate that, in this case, the combined $-I$ and $-I'$ effects outweigh the $+M$ effects, thus leading to overall electron-recession facilitating the reaction, and that here $-(-I, +M)_{Thienyl} < -(-I, +M)_{Furyl}$ (the signs in front of the bracket are not used algebraically, but to signify that the overall effects are negative, *i.e.*, electron-attractive). It is not readily apparent why the relative magnitudes of the $-I$ and $+M$ effects should be reversed in the heterocyclic groups, nor can the difficulties be solved by recourse to a $-E$ effect involving the expansion of valency shell of the sulphur atom to a decet of electrons in the transition state, since if this were large it would make the total electron-attractive influence of the thienyl group larger than that of the furyl group. The most reasonable explanation seems to be that the $+M$ effects are considerably smaller for the heterocyclic groups than for the *p*-methoxyphenyl and methylthiophenyl groups relatively to phenyl, *i.e.*, that the permanent resonance interaction between the heterocyclic and the CO_2R group is smaller than that between the aryl and the CO_2R group. This deduction is open to experimental test, but the required data are not at present available.

Experimental

The kinetic measurements were carried out by the technique previously described (Braude and Fawcett, *J.*, 1950, 800), the rates of rearrangement being determined by following the changes in ultra-violet light absorption intensity at the wave-lengths at which the rearranged isomers exhibit their characteristic maxima. The alcohols were those described in the preceding paper. The final absorption curves and intensities in solution agreed within experimental error with those of the rearranged isomers determined separately, showing that, under the conditions chosen, the rearrangements went to over 98% completion and were not accompanied by dehydration or other side-reactions. (The absolute values of the wave-length and intensities of the maxima differ slightly from those given in the preceding paper which were determined on a Hilger photographic instrument; in the present work, a Beckman photoelectric instrument

Rearrangements of 1-2′-*furyl*-3-*methylallyl alcohol.*

(i) In 0·001M-hydrochloric acid, 60% (by vol.) dioxan–water at 30°. Alcohol concn. 0·0044 mole/l.

Time (min.) ...	0	2	3	4	6	8	60	
$E^{1\%}_{1\ cm.}$ (2640 Å) ...	24	395	543	657	854	993	1342	
10^4k (min.$^{-1}$) ...	—	1660	1670	1640	1660	1650	—	(Mean) 1660

(ii) In 0·001M-hydrochloric acid, 80% (by vol.) dioxan–water at 30°. Alcohol concn. 0·0048 mole/l.

Time (min.) ...	0	4	6	8	10	12	80	
$E^{1\%}_{1\ cm.}$ (2640 Å)	24	383	510	649	760	834	1368	
10^4k (min.$^{-1}$) ...	—	785	750	782	790	767	—	(Mean) 775

(iii) In 0·001M-hydrochloric acid, 60% (by vol.) dioxan–water at 50°. Alcohol concn. 0·0049 mole/l.

Time (sec.)	0	25	47	68	87	105	127	1200	
$E^{1\%}_{1\ cm.}$ (2640 Å)	24	473	750	930	1038	1115	1165	1320	
10^4k (min.$^{-1}$) ...	—	10,200	10,500	10,600	10,500	10,300	10,800	—	(Mean) 10,500

Rearrangements of 3-*methyl*-1-2′-*thienylallyl alcohol.*

(i) In 0·001M-hydrochloric acid, 60% (by vol.) dioxan–water at 30°. Alcohol concn. 0·0061 mole/l.

Time (min.)	0	3	6	9	12	15	180	
$E^{1\%}_{1\ cm.}$ (2780 Å) ...	100	241	362	465	543	612	930	
10^4k (min.$^{-1}$) ...	—	644	630	637	633	638	—	(Mean) 636

(ii) In 0·001M-hydrochloric acid, 80% (by vol.) dioxan–water at 30°. Alcohol concn. 0·0056 mole/l.

Time (min.)	0	15	20	25	30	35	240	
$E^{1\%}_{1\ cm.}$ (2780 Å) ...	26	350	422	489	546	595	923	
10^4k (min.$^{-1}$)	—	296	291	290	289	288	—	(Mean) 291

(iii) In 0·001M-hydrochloric acid, 60% (by vol.) dioxan–water at 50°. Alcohol concn. 0·0060 mole/l.

Time (sec.)	0	18	37	52	67	82	540	
$E^{1\%}_{1\ cm.}$ (2780 Å) ...	26	244	411	527	605	667	875	
10^4k (min.$^{-1}$)	—	9900	9800	10,200	10,500	10,300	—	(Mean) 10,100

was employed.) The plots of the logarithms of the rate-constants at different temperatures against $1/T$ were satisfactorily linear. Six typical runs are reproduced above; in several cases the values of k differ slightly from those given in Table 1 which were averaged from duplicate runs.

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802. *Interaction of Aromatic Ketones with Aluminium Chloride.*

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The products of interaction of aluminium chloride with the 2 : 5-di-*n*-propyl derivatives of acetophenone and propiophenone and with 2 : 5- and 2 : 4-di*iso*propylacetophenone are reported. Dealkylation accompanies isomerisation and a means is revealed of obtaining 3-alkyl- and 3 : 5-dialkylphenyl ketones; these reactions are compared with those obtained with 2 : 5-dimethyl- and 2 : 5-diethyl-phenyl ketones.

2 : 4- and 2 : 5-Di*iso*propylacetophenone have been prepared by acetylation of *p*-di*iso*propylbenzene below 5° in ethylene chloride and carbon disulphide respectively. Both these ketones afford acetophenone and its 4-*iso*propyl derivative when fused with aluminium chloride at 100°.

Partial dealkylation of several 4-alkylacetophenones is reported.

ONE of us has reported (*J.*, 1944, 232) that interaction of *o*-methyl- and *o*-ethyl-aryl ketones with excess of aluminium chloride effects mainly isomerisation (80%) and that the pro-

ducts are determined by the relative rates of (i) deacylation followed by reacylation, and (ii) intramolecular migration of the *o*-alkyl group to the adjacent *meta*-position. This work has been extended to include aryl ketones containing other *o*-alkyl groups and we now report the action of aluminium chloride on the 2 : 5-di-*n*-propyl derivatives of acetophenone and propiophenone and on 2 : 5- and 2 : 4-di*iso*propylacetophenone. Each of these ketones, in marked contrast to those in the earlier work, provides mainly tars by interaction at temperatures above 120° and, in consequence, a temperature of 100° was selected. The products are listed in the Table, where some obtained in the earlier work are included for comparison.

Acylation of *p*-di-*n*-propylbenzene, like that of *p*-diethylbenzene and *p*-xylene, readily affords the corresponding 2 : 5-dialkylphenyl ketone; on the other hand, 2 : 4-di*iso*propylacetophenone is obtained by interaction of *p*-di*iso*propylbenzene with acetic anhydride and aluminium chloride in boiling carbon disulphide (Newton, *J. Amer. Chem. Soc.*, 1943, **65**, 2444). We find that acetyl chloride in carbon disulphide affords the 2 : 5-isomer when the temperature of reaction is below 5° but that the 2 : 4-isomer is obtained even at these temperatures when ethylene chloride is the solvent. Both ketones were identified by deacetylation with syrupy phosphoric acid at 180° and preparation of the sulphonamides of the resulting hydrocarbons. It is unlikely that the above preparation

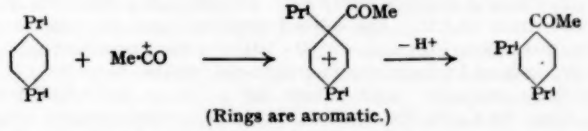
Products of interaction with excess of aluminium chloride at 100° *for* 18 *hours.*

Initial ketone	Products
2 : 5-$C_6H_3Pr_2$·COMe ...	C_6H_5·COMe (3%) + *m*-C_6H_4Pr·COMe (43%) + 3 : 5-$C_6H_3Pr_2$·COMe (24%)
2 : 5-$C_6H_3Pr_2$·COEt ...	C_6H_5·COEt (4%) + *m*-C_6H_4Pr·COEt (36%) + 3 : 5-$C_6H_3Pr_2$·COEt (29%)
2 : 5-$C_6H_3Pr^i_2$·COMe ...	C_6H_5·COMe (27%) + *p*-$C_6H_4Pr^i$·COMe (27%)
*2 : 5- ,, ...	*m*- ,, (65%) + 3 : 5-$C_6H_3Pr^i_2$·COMe (24%)
2 : 4- ,, ...	C_6H_5·COMe (15%) + *p*- ,, (34%)

	Temp.	Time (hrs.)	Products
2 : 5-$C_6H_3Me_2$·COMe ...	150°	1·5	3 : 5 (77%) + 3 : 4-$C_6H_3Me_2$·COMe (8%)
2 : 5-$C_6H_3Et_2$·COMe ...	150	1·25	3 : 5-$C_6H_3Et_2$·COMe (88%)
p-C_6H_4Me·COMe	205	1	C_6H_5·COMe (0%) + Initial ketone (80%)
p-C_6H_4Et·COMe	205	1	,, (7%) + ,, (45%)
p- ,, ...	160	4	,, (2%) + ,, (75%)
p-C_6H_4Pr·COMe	205	0·75	,, (7%) + ,, (48%)
p- ,, ...	100	18	,, (6%) + ,, (64%)

* In Ethylene chloride at room temperature.
In each instance the rest of the material is non-volatile.

of 2 : 4-di*iso*propylacetophenone depends on the isomerisation of the 2 : 5-isomer since this, in the presence of hydrogen and aluminium chlorides and in ethylene chloride, provides a mixture of *m*-*iso*propyl- and 3 : 5-di*iso*propyl-acetophenone; these ketones have not been described previously and were identified by oxidation to *iso*phthalic and trimesic acid respectively (see Experimental section); apparently, 2 : 4-di*iso*propylacetophenone is obtained directly from the acetylation of *p*-di*iso*propylbenzene :



(Rings are aromatic.)

This formulation is compatible with the formation of *p*-*tert.*-butylacetophenone from *p*-di-*tert.*-butylbenzene by the action of acetyl chloride and aluminium chloride (Hennion and McLeese, *ibid.*, 1942, **64**, 2421); the *tert.*-butyl group is eliminated whereas migration of the *iso*propyl group is intramolecular. Substitution in the position *ortho* to these bulkier alkyl groups seems to encounter considerable steric hindrance.

2 : 5-Di-*n*-propyl-acetophenone and -propiophenone behave similarly when fused with aluminium chloride at 100°. In each instance, the product of reaction distils over a wide

range of temperature and the distillate, representing 70% of the initial ketone, consists of the 3 : 5-di-*n*-propylphenyl ketone (*ca.* 38%) and the *m*-*n*-propylphenyl ketone (*ca.* 58%); these are afforded respectively by migration and elimination of the *o*-propyl group. The latter process, which provides the major product of the reaction, is not a feature of the interaction of 2 : 5-dimethylacetophenone with aluminium chloride; in this instance, the distillate is obtained over a small range of temperature and consists entirely of isomeric material; 2 : 5-diethylacetophenone, though similar in its behaviour to the 2 : 5-dimethyl derivative, does suffer some (*ca.* 3%) dealkylation.

An *o*-*iso*propyl group is still more readily eliminated than an *o*-*n*-propyl group and 2 : 5- and 2 : 4-di*iso*propylacetophenone afford only products of dealkylation, together with much tar, when fused with aluminium chloride at 100°; as mentioned above, *m*-*iso*propyl- and 3 : 5-di*iso*propyl-acetophenone are obtained in yields of 65 and 24% respectively from the 2 : 5-isomer in ethylene chloride at room temperature. These results show that ease of elimination of the alkyl group increases in the order $Me<Et<Pr^{n}<Pr^{i}$; this is compatible with the possibility that the alkyl group is eliminated as a cation. Other data in the Table show that elimination of an alkyl group is, though to a less extent, a feature of *m*- and *p*-alkylphenyl ketones.

Since acetophenone and its homologues have been alkylated by the Friedel–Crafts method (*J.*, 1949, S 229) and since dealkylation of 2 : 5-di-*n*-propyl-acetophenone and -propiophenone affords *m*-*n*-propyl-acetophenone and -propiophenone, there was the possibility that these might provide 3 : 5-dipropylphenyl ketones by interaction with propyl cations. This process does not occur since it would involve isomerisation of the propyl group and would provide 3-*n*-propyl-5-*iso*propylphenyl ketones, whereas, in fact, 3 : 5-di-*n*-propylphenyl ketones are obtained; it thus seems that these ketones, like 3 : 5-dimethyl- and 3 : 5-diethyl-phenyl ketones, are obtained from the corresponding 2 : 5-isomers by intramolecular migration of the *o*-alkyl group.

The 3 : 5-di-*n*-propyl derivatives of acetophenone and propiophenone were identified by oxidation to trimesic acid and reduction by the Clemmensen method to benzene homologues which, when polybrominated at 0° with liquid bromine in the presence of iron powder, afforded tribomo-derivatives without loss of an alkyl group; this established the configuration of the propyl groups since Hennion and Anderson (*J. Amer. Chem. Soc.*, 1946, **68**, 424) have shown that bromination under these conditions displaces secondary and tertiary but not primary alkyl groups. The *m*-*n*-propyl derivatives of acetophenone and propiophenone were identified by comparison with authentic samples.

Should the results obtained in the cases of the 2 : 5-di-*n*-propyl- and 2 : 5-di*iso*propylphenyl ketones be reproducible when the propyl and *iso*propyl groups are replaced by other normal and secondary alkyl groups, a ready means of obtaining *m*-alkyl- and 3 : 5-dialkylphenyl ketones will be available.

Experimental

Ketones.—2 : 5-Di-*n*-propylacetophenone was obtained by gradual addition of *p*-di-*n*-propylbenzene (60 g.) to an ice-cold mixture of aluminium chloride (78 g., 1·5 mols.) and acetyl chloride (37 g., 1·25 mols.) in ethylene chloride (400 c.c.). The product was poured on ice, the organic layer separated and dried (K_2CO_3), the solvent removed, and the residue was fractionally distilled. The required ketone (51 g.), b. p. 100—101°/0·1 mm., provided a 2 : 4-dinitrophenylhydrazone which crystallised from ethanol in orange-red needles, m. p. 75° (*J.*, 1944, 232).

2 : 5-*Di*-n-*propylpropiophenone*. This ketone (55 g.), b. p. 112—116°/0·5 mm. (Found : C, 82·1; H, 9·8. Calc. for $C_{15}H_{22}O$: C, 82·5; H, 10·1%), was similarly obtained from di-*n*-propylbenzene (60 g.) and propionyl chloride (44 g.) (Baddeley and Kenner, *J.*, 1935, 303).

2 : 5-*Diiso*propylacetophenone. *iso*Propylbenzene (50 g.), obtained by interaction of sodium-dried benzene (350 c.c.) and *iso*propyl bromide (79 g.) in the presence of aluminium chloride (10 g.) (Vogel, " Practical Organic Chemistry," p. 494, Longmans, Green and Co., London, 1948), was added to a mixture of aluminium chloride (90 g., 1·5 mols.) and acetyl chloride (42 g., 1·25 mols.) in ethylene chloride (350 c.c.). The resulting *p*-*iso*propylacetophenone (59 g.) was a pale yellow oil, b. p. 115°/10 mm., which afforded an oxime, m. p. 71° (Widman, *Ber.*, 1888, **21**, 2226), and a *semicarbazone*, m. p. 200—202° (Found : C, 66·1; H, 7·8; N, 19·3.

$C_{12}H_{17}ON$ requires C, 65·8; H, 7·8; N, 19·2%) after crystallisation from ethanol. This ketone (54 g.) in dry ether (75 c.c.) was gradually added to a solution of magnesium (12·2 g.) and methyl iodide (71 g.) in ether (250 c.c.). The mixture was stirred at room temperature for 2 hours and poured into an ice-cold solution of ammonium chloride (100 g.) in water (600 c.c.); the ethereal layer, together with two ether-extracts of the aqueous layer, was washed with water and dried (K_2CO_3). Distillation afforded 2-p-iso*propylphenylpropan*-2-*ol* (48 g.), b. p. 118—119°/10 mm., m. p. 38° (Found: C, 80·5; H, 9·6. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1%). This alcohol (45 g.) was touched with a glass rod which had been moistened with dilute sulphuric acid and rapidly distilled under reduced pressure from an oil-bath preheated to 125°. *p-iso*Propenyl-*iso*propylbenzene (38 g.) was obtained as a mobile oil, b. p. 96—100°/12 mm.; it was reduced by hydrogen and Raney nickel in methanol to *p*-di*iso*propylbenzene (36 g.), b. p. 87—89°/15 mm. (sulphonamide, m. p. 109°; Newton, *loc. cit.*, records m. p. 110·2—110·8°), n_D^{15} 1·4910 (Ipatieff and Pines, *J. Amer. Chem. Soc.*, 1932, **54**, 674, record n_D^{20} 1·4907). A mixture of this hydrocarbon (50 g.) and acetyl chloride (27 g.) was slowly added to a vigorously stirred mixture of aluminium chloride (45 g.) and carbon disulphide (60 c.c.) at −5°; the mixture was stirred for 4 hours and the temperature allowed to rise to 5°. The mixture was decomposed with ice, and the carbon disulphide layer was separated, dried (K_2CO_3), and distilled. Initial hydrocarbon (8 g.), b. p. 55—65°/0·05 mm., and 2 : 5-*di*iso*propylacetophenone* (35 g.), b. p. 92—95°/0·1 mm., n_D^{18} 1·5120 (Found: C, 82·0; H, 9·5. $C_{14}H_{20}O$ requires C, 82·3; H, 9·8%), were obtained. This ketone afforded a *semicarbazone*, m. p. 165° (Found: C, 69·3; H, 8·6; N, 16·5. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%), which crystallised from ethanol. The ketone (2 c.c.) was refluxed with syrupy phosphoric acid (b. p. 180°) for 8 hours and the mixture distilled with steam; the organic material was separated, dried, and heated with concentrated sulphuric acid (2 c.c.) at 100° until a homogeneous solution was obtained. This was poured into water, and the mixture extracted with ether; the aqueous layer was neutralised with barium carbonate, filtered from barium sulphate, and freed from barium ions by addition of sodium sulphate solution. The aqueous solution was evaporated to dryness and the sodium salt heated with phosphorus pentachloride; the mixture was extracted with light petroleum, the extract washed with water, the solvent removed, and the residue heated with aqueous ammonia (*d* 0·88); the sulphamyl derivative, m. p. and mixed m. p. 110°, of p-di*iso*propylbenzene was obtained.

2 : 4-*Di*iso*propylacetophenone*. A mixture of *p*-di*iso*propylbenzene (63 g.) and acetyl chloride (33 g.) was gradually added to a vigorously stirred mixture of aluminium chloride (57 g.) and ethylene chloride (60 c.c.) at −5° and then kept overnight, the temperature gradually rising to room temperature. The mixture was decomposed with ice and worked up in the usual way; it afforded a fraction (14 g.), b. p. 69—93°/0·2 mm., 2 : 4-di*iso*propylacetophenone (39 g.), b. p. 93—97°/0·2 mm., and a residue which crystallised from light petroleum in colourless needles, m. p. 103° (Found: C, 82·1; H, 10·2%). The required ketone formed a semicarbazone, m. p. 196°, from ethanol (Newton, *loc. cit.*) and afforded 2 : 4-di*iso*propylbenzene (sulphonamide, m. p. 144—145°; cf. *idem*, *loc. cit.*), when deacetylated with syrupy phosphoric acid.

m-n-Propylpropiophenone was prepared as described by Baddeley and Kenner (*loc. cit.*); its semicarbazone melted at 132° and not at 128° as reported by them.

m-n-Propylacetophenone was obtained by interaction of methylmagnesium iodide and *m-n*-propylbenzonitrile; it afforded a *semicarbazone*, m. p. 170° (Found: C, 65·3; H, 7·8; N, 19·3. $C_{12}H_{17}ON_3$ requires C, 65·8; H, 7·8; N, 19·2%).

Interactions with Excess of Aluminium Chloride.—Procedure. A mixture of ketone and aluminium chloride (3 mols.) was heated at 100° for 18 hours; it formed a fluid melt and little chloride remained undissolved. After decomposition with ice, the mixture was extracted repeatedly with ether, and the extracts were dried (K_2CO_3) and distilled.

2 : 5-*Di*-n-*propylacetophenone*. This (50 g.) and aluminium chloride (100 g.) afforded a brown mixture which slowly evolved hydrogen chloride during the first hour and remained mobile. Ketonic material (33 g.), b. p. 55—105°/0·2 mm., was obtained; it afforded the following fractions: (i) acetophenone (0·8 g.), b. p. 53—57°/0·15 mm. (semicarbazone, m. p. and mixed m. p. 198°); (ii) *m-n*-propylacetophenone (17·0 g.), b. p. 70—85°/0·2 mm. (semicarbazone, m. p. and mixed m. p. 170°) [oxidation with chromic acid (Hennion and McLeese, *loc. cit.*) gave *iso*phthalic acid, identified as its dimethyl ester, m. p. and mixed m. p. 64°]; and (iii) 3 : 5-*di*-n-*propylacetophenone* (11·8 g.), b. p. 100—105°/0·2 mm. The last ketone formed a 2 : 4-*dinitrophenylhydrazone*, red needles (from ethanol), m. p. 130° (Found: C, 62·8; H, 6·3; N, 14·6. $C_{20}H_{24}O_4N_4$ requires C, 62·5; H, 6·3; N, 14·6%), and with nitric acid (Aitken, Badger, and Cook, *J.*, 1950, 331) afforded trimesic acid, m. p. 364° (trimethyl ester, m. p. and mixed m. p. 143°); oxidation with alkaline hypochlorite and with selenium dioxide and hydrogen

peroxide (Arnold and Rondesvedt, *J. Amer. Chem. Soc.*, 1945, **67**, 1265) afforded a waxy acid, m. p. 43° [Found : equiv., 202. Calc. for $(C_3H_7)_2C_6H_3 \cdot CO_2H$: equiv., 206]; Clemmensen reduction gave a *hydrocarbon* which was added to a mixture of bromine and iron powder (see Hennion and Anderson, *loc. cit*), yielding a viscous oil, whose bromine content was determined by Viebock's method (*Ber.*, 1932, **65**, 586) (Found : Br, 55·7. $C_{14}H_{19}Br_3$ requires Br, 56·2%).

2 : 5-*Di*-n-*propylpropiophenone*. This (50 g.) and aluminium chloride (100 g.) afforded a brown mixture which slowly evolved hydrogen chloride during the first hour and remained mobile. Ketonic material (33·3 g.), b. p. 70—120°/0·1 mm., was obtained; it afforded (i) propiophenone (1·2 g.), b. p. 67—85°/0·1 mm. (semicarbazone, m. p. and mixed m. p. 172°); (ii) *m-n*-propylpropiophenone (14·6 g.), b. p. 90—100°/0·1 mm. [semicarbazone, m. p. and mixed m. p. 128° (Found : N, 18·1. Calc. for $C_{13}H_{19}ON_3$: N, 18·0%)]; and (iii) 3 : 5-*di*-n-*propylpropiophenone* (14·7 g.), b. p. 115—120°/0·1 mm., which formed a 2 : 4-*dinitrophenylhydrazone*, red needles (from acetic acid), m. p. 133° (Found : N, 14·1. $C_{21}H_{26}O_4N_4$ requires N, 14·1%), with nitric acid afforded trimesic acid, m. p. 364° (trimethyl ester, m. p. and mixed m. p. 143°), and by Clemmensen reduction gave a hydrocarbon which, as above, gave 2 : 4 : 6-*tribromo*-1 : 3 : 5-*tri*-n-*propylbenzene*, colourless needles (from ethanol), m. p. 111° (Found : C, 41·3; H, 4·8; Br, 54·5. $C_{15}H_{21}Br_3$ requires C, 40·9; H, 4·8; Br, 54·4%).

2 : 5-*Di*iso*propylacetophenone*. This (7 g.) and aluminium chloride (14 g.) afforded a brown mixture which rapidly darkened and became almost black; hydrogen chloride was evolved during the whole of the period of heating. Distillable ketonic material (2·8 g.), b. p. 45—88°/0·1 mm., and residual black tar were obtained; the former afforded (i) acetophenone (1·1 g.), b. p. 45—50°/0·1 mm., m. p. 15° (semicarbazone, m. p. and mixed m. p. 198°), and (ii) b. p. 84—88°/0·2 mm. (0·8 g.). Fraction (ii) was a mixture (semicarbazone, m. p. 157—162° after repeated recrystallisation); it contained, apparently, *p-iso*propylacetophenone since oxidation by chromic acid afforded terephthalic acid (dimethyl ester, m. p. and mixed m. p. 140°).

2 : 4-*Di*iso*propylacetophenone*. This (37 g.) and the chloride (74 g.) afforded a brown mixture which rapidly darkened until almost black; hydrogen chloride was evolved throughout the heating. Distillable ketonic material (16 g.) was obtained and afforded acetophenone (3·2 g.), b. p. 48—52°/0·05 mm. (semicarbazone, m. p. and mixed m. p. 198°), and *p-iso*propylacetophenone (10·1 g.), b. p. 80—83°/0·1 mm. [semicarbazone, m. p. and mixed m. p. 200°; with chromic acid provided terephthalic acid (dimethyl ester, m. p. and mixed m. p. 140°)].

Isomerisation of 2 : 5-*Di*iso*propylacetophenone in Ethylene Chloride at* 15°.—Finely powdered aluminium chloride (21 g.) was gradually added to a cooled solution of the ketone (20 g.) in ethylene chloride (50 c.c.); a little chloride remained undissolved. The mixture was saturated with dry hydrogen chloride and set aside at 15° for 18 hours. The mixture was decomposed with ice, and the organic layer was separated, dried (K_2CO_3), and distilled. The following fractions were obtained : (i) m-iso*Propylacetophenone* (10·3 g.), b. p. 84—90°/0·2 mm. (Found : C, 81·8; H, 9·0. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%); this afforded a *semicarbazone*, m. p. 170°, from ethanol (Found : C, 65·3; H, 7·5; N, 18·6. $C_{12}H_{17}ON_3$ requires C, 65·8; H, 7·8; N, 19·2%), which depressed the m. p. (170°) of the semicarbazone of *m-n*-propylacetophenone; oxidation with nitric acid afforded *iso*phthalic acid, identified as its dimethyl ester, m. p. and mixed m. p. 64°. (ii) A fraction, b. p. 95—105°/0·2 mm. (4·7 g.), which apparently contains 3 : 5-di*iso*propylacetophenone since oxidation with nitric acid gave trimesic acid which was identified as its trimethyl ester. This fraction, with 2 : 4-dinitrophenylhydrazine, provided red crystals, m. p. 117—122°, unaffected by repeated recrystallisation from ethanol and glacial acetic acid.

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803. *The Kinetics of Ionic Polymerisations. Part III.* The Side-chain Effect in the Vinyl Ethers.*

By D. D. Eley and J. Saunders.

This paper presents rate of polymerisation and molecular-weight data for the system alkyl vinyl ether–iodine, in diethyl ether solvent at 25°.

The side groups examined are: *cyclo*hexyl, *iso*butyl, 2-ethylhexyl, *n*-butyl, ethyl, and 2-chloroethyl. The initial velocities at low values of [M] fit the expression $v = k[I_2]^2[M]$, where [M] denotes monomer concentration, but reach a maximum value at a certain value of [M], *viz.*, $[M]_t$. It is postulated that a part of the iodine is bound as a complex with the monomer (Type II complex), which is inactive in initiating polymerisation. The percentage of inactive complex increases with monomer concentration, and the $[M]_t$ value may be explained in terms of the formation equilibrium constant for the inactive complex, K_c; k, and to a less extent K_c, increase as one passes to side groups with a greater electron-repulsive effect, but the degree of polymerisation of the product shows no systematic variation. These results fit in with the expectations for the individual kinetic steps concerned in the chain reaction.

The catalytic action of iodine in polymerising ethyl vinyl ether was discovered by Wislicenus (*Annalen*, 1878, **192**, 106) and further investigated by Chalmers (*Canadian J. Res.*, 1932, *B*, **7**, 464). Eley and Richards (*Trans. Faraday Soc.*, 1949, **45**, 425) established the kinetics for the polymerisation of 2-ethylhexyl vinyl ether in three solvents and postulated that the polymerisation involved carbonium ions and was initiated by I^+. In this paper, we examine quantitatively the effect of the nature of the side chain R, in $RO{\cdot}CH{:}CH_2$, on the rate of polymerisation and the molecular weight of the product. In the discussion we show that the results obtained may be fitted into the kinetic scheme advanced by Eley and Richards, with one addition.

Experimental

The rate of polymerisation was followed in an evacuated, sealed, dilatometer at 25°. Densities of monomer and polymer were determined, so that the initial rate of volume change could be converted into a reaction velocity in moles $l.^{-1}$ $min.^{-1}$.

The polymer densities were determined separately for every specimen, usually with a micropyknometer but in the case of solids by a flotation method. Average values are listed in Table 1. The monomer densities agree with such values as are given in the literature (Schildknecht, Zoss, and McKinley, *Ind. Eng. Chem.*, 1947, **39**, 180).

Table 1. *Polymerisation of vinyl ethers.*

No.	Side chain	ρ_m	ρ_p	$[I_2]$	k	$[M]_t$	v_t
1	*cyclo*Hexyl	0·878	1·019	4·37	22,000	0·8	0·32
2	*iso*Butyl	0·764	0·902	4·37	1,900	0·8	0·025
3	2-Ethylhexyl	0·812	0·866	4·37	1,000	1·5	0·027
4	*n*-Butyl	0·774	0·905	4·37	1,800	1·8	0·052
	,,	—	—	2·18	1,800	(1·8)	0·01
	,,	—	—	5·47	1,800	3·0	0·073
5	Ethyl	0·748	0·937	4·37	1,900	3·2	0·09
6	2-Chloroethyl	1·039	1·234	4·37	90	>4·3	>0·007

The order in which the electron-repulsive effect of the side chain decreases is from 1 to 6, so far as can be judged from published data on reactions of ions with aliphatic carbon atoms.

The reactions were stopped at 20—30% of polymerisation, the dilatometer opened, the catalyst destroyed with thiosulphate, and the polymer isolated according to Eley and Richards (*loc. cit.*). The molecular weight was determined from the freezing-point depression Δ in benzene. This was determined at a range of concentrations c, and Δ/c plotted against c so as to allow extrapolation to obtain $(\Delta/c)_{c\to 0}$, which was used in the calculation.

* Part II, *Trans. Faraday Soc.*, 1949, **45**, 436.

In all experiments, the polymerisations were carried out with diethyl ether as solvent, so as to obviate any marked change in the dielectric constant of the system as the reaction progressed.

Reaction Velocity.—The reaction curve was accurately linear over the first 10% of

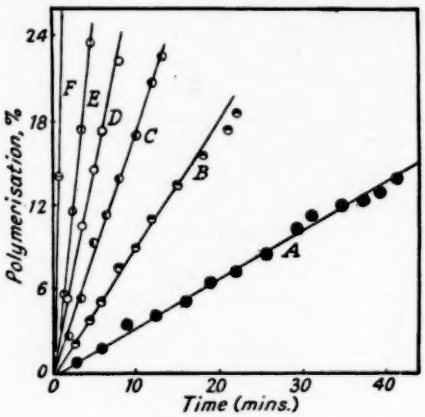


FIG. 1. *Polymerisation–time relationships for* n-*butyl vinyl ether.* ([M] = 0·86 mole/l. Curve *A*, [C] = 1·10; curve *B*, [C] = 2·19; curve *C*, [C] = 3·29; curve *D*, [C] = 3·84; curve *E*, [C] = 5·47, and curve *F*, [C] = 10·95 mmole/l.)

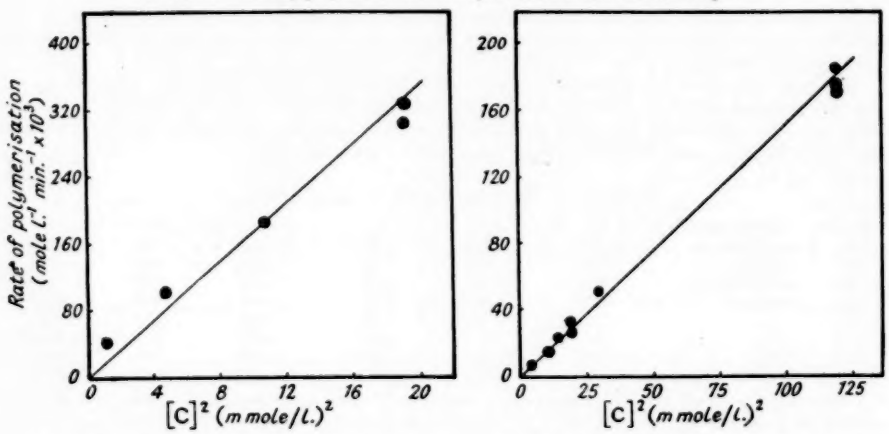
polymerisation and passed through the origin, showing an absence of any induction period. An example is shown in Fig. 1.

The reaction velocity was examined as a function of monomer concentration [M] and catalyst concentration $[I_2]$. At low monomer concentrations, the initial velocities v fit the equation

$$v = -\mathrm{d}[\mathrm{M}]/\mathrm{d}t = k[\mathrm{M}][\mathrm{I}_2]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

in agreement with Eley and Richards (*loc. cit.*). All the results are presented graphically for convenience. Figs. 2*a* and 2*b* show that the reaction velocity is proportional to $[I_2]^2$ in two cases, confirming the work of Eley and Richards on the 2-ethylhexyl ether.

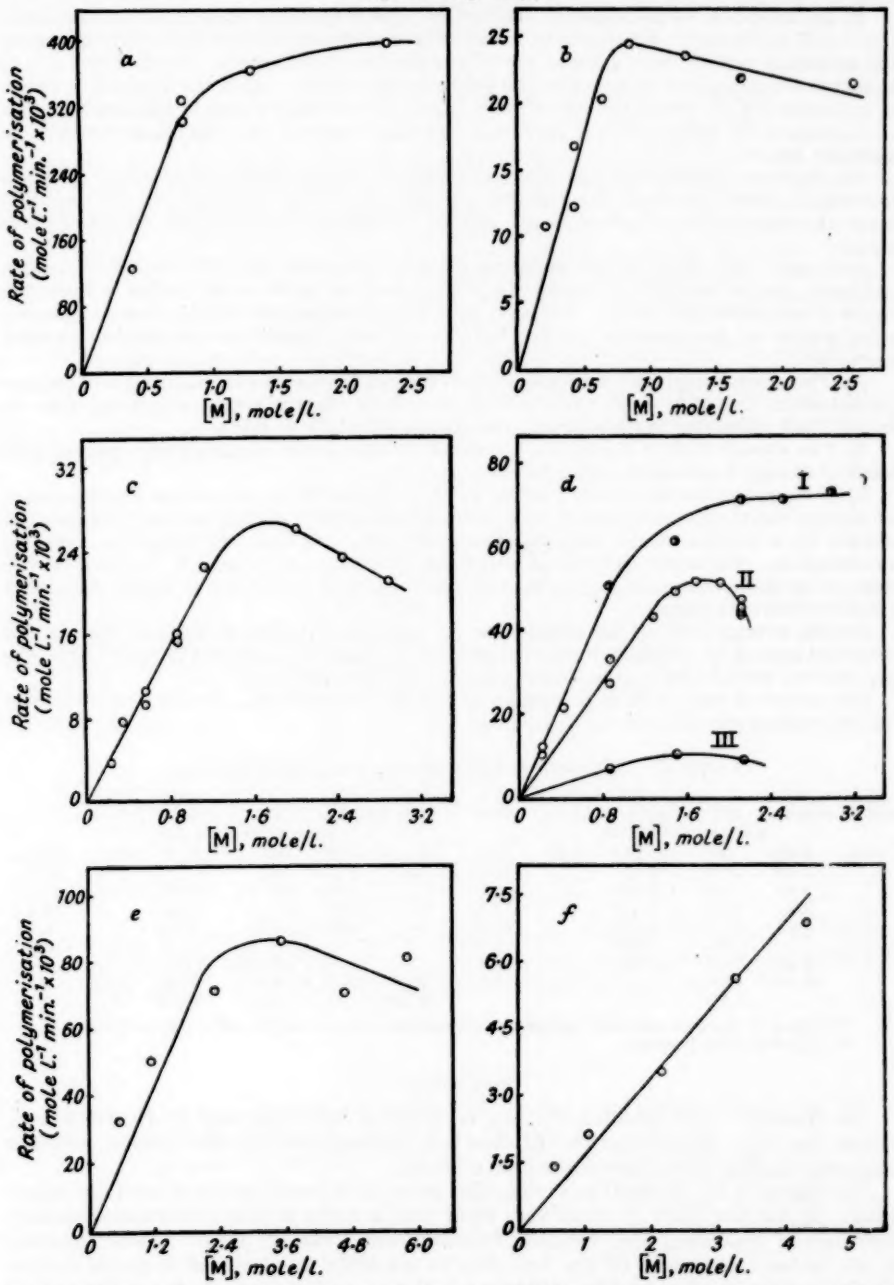
FIG. 2*a–b*. *Rate of polymerisation–catalyst concentration relationships.*



(*a*) cyclo*Hexyl vinyl ether* ([M] = 0·774 mole/l.). (*b*) n-*Butyl vinyl ether* ([M] = 0·86 mole/l.).

The effect of monomer concentration is considered for all the cases examined in Figs. 3*a—f* inclusive. It is seen that, for the 2-chloroethyl vinyl ether, $v \propto [\mathrm{M}]$ over the whole range up to [M] = 4·3 mole/l. For the other ethers, there is a fairly definite value of [M], designated $[\mathrm{M}]_t$, at which the reaction velocity reaches a maximum value, v_t. In the case of 2-ethylhexyl ether, Eley and Richards failed to reach a high enough [M] value to find the maximum velocity. We

FIG. 3. *Rate of polymerisation–monomer concentration relationships.* [C] = 4·37 *millimole per litre throughout, except in* (*d*).



(*a*), cyclo*Hexyl vinyl ether*; (*b*), iso*butyl vinyl ether*; (*c*), 2-*ethylhexyl vinyl ether*; (*d*), n-*butyl vinyl ether* (curve I, [C] = 5·47; curve II, [C] = 4·37; and curve III, [C] = 2·19 mmole/l.); (*e*), *ethyl vinyl ether*; (*f*), 2-*chloroethyl vinyl ether*.

have confirmed two of their results at low values of [M], and made further experiments at high values of [M] to establish the curve shown.

In the first place, all the results on effect of [M] were obtained at the catalyst concentration, $[I_2] = 4{\cdot}37$ millimole/l. Subsequently, in one case, that of *n*-butyl vinyl ether, experiments on the maximum velocity were made at two other catalyst concentrations. In the table, ρ_m and ρ_p are the densities at 25° of monomer and polymer, respectively; $[I_2]$ is the total iodine added, in millimoles $l.^{-1}$; k, the third-order velocity constant, in $l.^2\ mole^{-2}\ min.^{-1}$; $[M]_t$ the monomer concentration, in moles $l.^{-1}$, for maximum velocity; and $[v]_t$ the maximum velocity, in moles $l.^{-1}\ min.^{-1}$.

The Polymers.—Most of the polymers were transparent viscous fluids, varying from colourless to orange, as found previously for 2-ethylhexyl vinyl ether. The *cyclo*hexyl vinyl ether gave a range of products from colourless liquids through colourless non-tacky solids to almost black solids.

Systematic work on cryoscopic molecular weights was carried out with *n*-butyl vinyl ether, *cyclo*hexyl vinyl ether and 2-chloroethyl vinyl ether, and the results are presented in Table 2 as degree of polymerisation (D.P.). The solid polymers are distinguished in the Table. There is a fair scatter in the cryoscopic results, but the following comments and conclusions seem warranted:

(*a*) The *n*-butyl vinyl ether was carefully investigated for the effect of monomer and catalyst concentration, and there would seem to be no systematic effect of either of these variables on degree of polymerisation of the product; the average value of D.P. is 9·8.

(*b*) The average D.P. of 4·6 for the 2-chloroethyl ether is not systematically changed by a four-fold change in monomer concentration.

(*c*) If we except the three lowest values of D.P., which relate to the viscous liquid product, the poly*cyclo*hexyl vinyl ethers are all solids with an average D.P. of about 16, not systematically affected by a ten-fold change in catalyst concentration or a four-fold change in monomer concentration. The rather high values of D.P. obtained may not be entirely comparable with those of the other two monomers, as the polymer could only be isolated at a later percentage polymerisation of monomer.

(*d*) The average D.P. of the product for the 2-chloroethyl ether is 4·6, and that for the *cyclo*hexyl ether is 16. This increase by a factor of 3—4 may be neglected in comparison with the observed 244-fold increase in overall velocity of polymerisation.

One sample of each of these polymers was tested for the presence of iodine with negative results, in agreement with Eley and Richards.

TABLE 2. *Molecular-weight data* (ca. 20% *polymerisation*).

[M], mole/l.	$[I_2]$, mmole/l.	D.P.	[M], mole/l.	$[I_2]$, mmole/l.	D.P.	[M], mole/l.	$[I_2]$, mmole./l.	D.P.	[M], mole/l.	$[I_2]$, mmole/l.	D.P.
n-Butyl vinyl ether						*cyclo*Hexyl vinyl ether *					
0·86	1·095	5·5	0·215	4·37	10·5	0·774	1·092	3·6	0·774	19·7	11·5 *s*
,,	2·19	11·0	0·43	,,	12·5	,,	2·185	6·7	,,	39·4	22·5 *s*
,,	3·29	9·5	1·288	,,	10·5	,,	3·278	16 *s* †	0·387	4·37	11·5 *s*
,,	3·84	12·5	1·504	,,	12·0	,,	4·37	21 *s*	1·548	,,	13·5 *s*
,,	4·37	7·5	1·717	,,	11·5	,,	4·37	18·2 *s*	2·322	,,	5·5
,,	,,	6·5	1·933	,,	9·0						
,,	5·47	10·0	2·149	,,	6·5	2-Chloroethyl vinyl ether					
,,	10·95	11·0	,,	,,	7·5	1·084	4·37	6·0	3·252	4·37	3·2
,,	,,	13·0				2·168	,,	4·2	4·336	,,	5·2

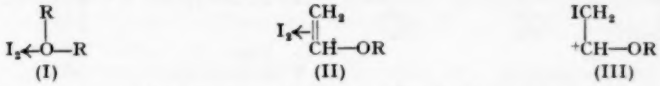
* Owing to speed of reaction, polymer could only be isolated at 60—80% polymerisation.
† *s* denotes solid polymer.

DISCUSSION

The Kinetics.—The equation (1) may be deduced from Eley and Richards's kinetic scheme (*loc. cit.*). To account for the observed maximum velocity at a certain monomer concentration $[M]_t$, the scheme requires an addition.

The nature of the interaction of molecular iodine with donor groups is not fully understood. In the first place, it seems very likely that it forms a weak co-ordinate link with ether oxygen (Kleinberg and Davidson, *Chem. Reviews*, **1948**, **42**, 601). This is suggested by the brown colour, and by the fact that its solubility is somewhat in excess of that calculated for a regular solution (Hildebrand, Benesi, and Mower, *J. Amer. Chem. Soc.*, **1950**, **72**, 1017). This complex is (I). In addition, we postulate a complex with the

ethylenic bond of the vinyl ether (II), by analogy with the complex $I_2 \ldots C_6H_6$ found spectroscopically for benzene by Benesi and Hildebrand (*ibid.*, 1949, **71**, 2703). Finally, we postulate a carbonium ion formed by addition of I^+ at one side of the double bond (III) in accordance with Eley and Richards's scheme.



(I) (II) (III)

There is no further need to consider (I) since all molecules present, monomer, solvent, and polymer, contain ether oxygen groups. We, therefore, have a more or less constant environment of oxygen donor atoms in space and time, and (I) may be assumed to be the normal state of all iodine not bound in (II) or (III) or as I_3^-. If the bond in (I) were at all strong, we should expect diethyl ether to be a slower solvent than light petroleum, whereas the reverse is the case. We may compare the addition of pyridine to the system, which *does* form a strong donor link to iodine and, according to our observations (to be published), completely inhibits the polymerisation.

We further assume that iodine bound in complex (II) is removed from the sphere of reaction, and is not free to ionise and hence form (III) and initiate reaction.

Let $[I_2]$ denote the total concentration of molecular iodine as added initially, [M] the total initial concentration of monomer, and x the concentration of inactive complex (II). We assume an equilibrium

$$(I) + RO{\cdot}CH{:}CH_2 \rightleftharpoons (II) + \text{ether}$$

which for the reason above we write simply as

$$I_2 + RO{\cdot}CH{:}CH_2 \rightleftharpoons (II)$$

and

$$x/[M]([I_2] - x) = K_c \text{ (l. mole}^{-1}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where we neglect the concentration of iodine bound in the reactive complex (III). Therefore the concentration of iodine free to initiate polymerisation, $[I_2]_f$, is

$$[I_2]_f = [I_2] - x = [I_2]/(1 + K_c[M]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The kinetic scheme is

$$\begin{aligned} 2I_2 &\longrightarrow I^+ + I_3^- && k_1 \\ I^+ + M &\longrightarrow I^+M = (III) && k_2 \\ I^+M + M &\longrightarrow M_2^* \\ M_{n-1}^* + M &\longrightarrow M_n^* && k_3 \\ M_n^* &\longrightarrow M_n && k_4 \\ M_n^* + M &\longrightarrow M_n + M^* && k_5 \end{aligned}$$

Assuming stationary concentrations of I^+ and M_n^*, we obtain as before (Eley and Richards, *loc. cit.*) a third-order equation, but with $[I_2]_f$ written in place of the total iodine concentration $[I_2]$. The two concentrations are related by equation (3). Hence

$$v = -d[M]/dt = k_1k_3[I_2]_f^2[M]/k_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and

$$\text{D.P.} = k_3[M]/(k_4 + k_5[M]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Equations (4) and (5) account satisfactorily for our results, since $[I_2]_f \sim [I_2]$, according to (3), at low monomer concentrations where $K_c[M] \ll 1$.

As the monomer concentration rises, we expect increasing amounts of iodine bound as the inactive complex (II). According to equation (2), the amount bound will depend on the mass-action constant K_c. This constant may be obtained from the monomer concentration for maximum velocity $[M]_t$, which by differentiation of the rate equation (4) and substitution for $[I_2]_f$ according to equation (3), is found to be

$$K_c = 1/[M]_t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Thus we arrive at the values of K_c given in Table 3.

TABLE 3. *Equilibrium constant for inactive complex.*

No.	Side chain	$[I_2]$, mmole l.$^{-1}$	K_c, l. mole^{-1}	No.	Side chain	$[I_2]$, mmole l.$^{-1}$	K_c, l. mole^{-1}
1	*cyclo*Hexyl	4·37	1·25	4	*n*-Butyl	4·37	0·5
2	*iso*Butyl	4·37	1·25		,,	2·18	(0·5)
3	2-Ethylhexyl	4·37	0·67		,,	5·47	0·33
				5	Ethyl	4·37	0·31
				6	2-Chloroethyl	4·37	<0·23

These values of K_c are rather larger than the iodine–benzene equilibrium constant given by Benesi and Hildebrand (*loc. cit.*), when converted into l. mole^{-1}.

In the case of the *n*-butyl ether, reference to Fig. 3 shows that the value of $[M]_f$ increases as the catalyst concentration increases so that the K_c value varies somewhat. There are not sufficient points accurately to define the shallow maximum at $[I_2] = 2{\cdot}18$ mmole l.$^{-1}$ so the K_c value is put in parentheses.

Effect of the Side Group R.—The side chains 1—6 in Tables 1 and 3 are numbered in order of their decreasing electron-repulsive effect. We are here concerned with the inductive effect, *i.e.*, the effect of the side chain on the reactivity of an aliphatic carbon atom to a positive (or negative) ion, and a survey of the literature of reactions of this type was made to establish the order for all common side chains. It seems clear that the overall reaction velocity constant k is much increased by an electron-repelling side chain, as we go from 2-chloroethyl (6) to *cyclo*hexyl (1). The exact order of groups 2—5, which lie rather close together so far as their inductive effect goes, may be influenced by the steric factor.

To supplement the above, we have the early observations that iodine will not catalyse the polymerisation of phenyl vinyl ether (Chalmers, *loc. cit.*) or divinyl ether. We should expect the vinyl group to be No. 7 in the list and markedly more electron-attractive than 2-chloroethyl. Thus, we should expect little or no reactivity for divinyl ether, but the phenyl group would be expected to give a somewhat more rapid polymerisation than 2-chloroethyl, as we should expect to fit it in between Nos. 5 and 6. The lack of activity to iodine may in part be explained by the co-ordination of the iodine to the phenyl ring, with a $K_c \sim 10^{-1}$ l. mole^{-1}, according to the work of Benesi and Hildebrand (*loc. cit.*). The phenyl vinyl ether may be polymerised with metallic halides and boron trifluoride (Favorskii and Shostakovskii, *J. Gen. Chem. U.S.S.R.*, 1943, **13**, 1; Losev, Fedotova, and Trostyanskaya, *ibid.*, 1945, **15**, 353).

The electron-repulsive effect of R in raising k may be due to either (*a*) rise in k_1, (*b*) rise in k_3, or (*c*) decrease in k_4. Since the vinyl ether does not enter into step 1, we can rule out (*a*). We have not specified the termination step 4, but this probably involves the expulsion of a positive ion, I^+ or H^+, and thus would be restrained by an electron-repulsive group as suggested. We may certainly expect (*b*) to operate, *i.e.*, the electron-repulsive group in the monomer will favour its reaction with a carbonium ion. We conclude that the effect observed is at any rate most probably due to a change in the ratio k_3/k_4.

It is also understandable that an electron-repulsive group R will raise the formation constant K_c for the inhibiting complex (II), and this is what is found (Table 3).

The Polymer.—The random variation in molecular weight values is somewhat larger than that found by Eley and Richards (*loc. cit.*), possibly owing to our use of the cryoscopic rather than the viscometric method. It seems clear that the observed D.P. is independent of catalyst and monomer concentrations, which agrees with equation (5) when one makes the proviso that transfer is important, so that $k_5[M] > k_4$, as found previously for the 2-ethylhexyl ether. This seems to hold not only for the case of *n*-butyl vinyl ether, but also for the extremely rapidly polymerising *cyclo*hexyl vinyl ether and the extremely slow 2-chloroethyl ether.

Since the D.P. is given by k_3/k_5, we can understand why a change in R from 2-chloroethyl to *cyclo*hexyl only increases the D.P. by at most a factor 4, while accelerating the overall rate 240-fold. The reaction k_5 is a reaction of active polymer with monomer, just as is k_3. We may, therefore, expect a similar effect of electron-repulsion in the side chain R on both reactions, leaving the ratio and therefore the D.P. almost unaffected.

Where spontaneous termination is active in ending the polymer chains, *i.e.*, $k_4 > k_5[M]$, it might be expected that for given conditions the *cyclo*hexyl vinyl ether will give a much higher molecular weight polymer than the 2-chloroethyl ether, since the ratio k_5/k_4 will be increased. We have considered that this condition holds for stannic chloride as catalyst, and the corollary is worth experimental test. It is clear from this discussion that, in any event, experiments on the effect of R may help to throw light on the question of termination mechanisms in controversial cases.

The polymer was isolated by destroying the catalyst with thiosulphate and removal of solvent and monomer under reduced pressure at 65—70°. Eley and Richards showed that the polymeric 2-ethyl hexyl vinyl ether so isolated did not contain any iodine and we confirm this for the *n*-butyl and the *cyclo*hexyl vinyl ether. By isolation at room temperature, a polymer containing roughly 0·5 double bond and 1·4 atoms of iodine was obtained. We take this to mean that the polymer probably contains one double bond per molecule, and that some iodine is held rather loosely, *e.g.*, possibly as di-iodide formed after the reaction, or a type (II) complex with a terminal double bond. Since transfer is operative, we should only expect one iodine atom in every $k_5[M]/k_4$ chains, even if an iodine atom were not lost in the termination step k_4. The results scarcely allow us to be definite at present, but since all the iodine dissociates easily from the polymer, it seems unlikely that any iodine is chemically bound, apart from the possibility of di-iodide formation by subsequent addition of iodine to a terminal double bond. This would mean that I^+ ions are lost in the termination step k_4, and if this is so, in order not to disturb our kinetic scheme, we need to postulate that $k_1[I_2]f^2 \gg k_4[M_n^+]$. This seems a reasonable assumption.

The authors thank Messrs. Erinoid, Limited, for a scholarship (1950—51) and Messrs. Courtaulds Scientific and Educational Trust Fund for a scholarship (1951—52), in each case to J. S., and Messrs. Courtaulds for a grant for apparatus.

THE UNIVERSITY, BRISTOL. [*Received, April 26th*, 1952.]

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804. *Carcinogenic Nitrogen Compounds. Part XII.* Fluorine-containing 1 : 2- and 3 : 4-Benzacridines.*

By NG. PH. BUU-HOÏ and PIERRE JACQUIGNON.

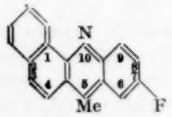
Four fluorine-containing 5-methyl-1 : 2- and -3 : 4-benzacridines have been synthesised by the modified Bernthsen reaction, for biological examination as potential carcinogenic agents. Several other new fluorinated compounds have also been prepared.

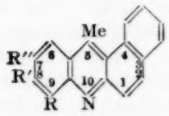
THE biological effect of introducing halogen into carcinogenic hydrocarbons and related compounds has rarely been investigated. Some chlorine-containing derivatives of 1 : 2-benzanthracene (Newman, *J. Amer. Chem. Soc.*, 1938, **60**, 1368; Newman and Orchin, *ibid.*, p. 586; 1939, **61**, 244; Shear and Leiter, *J. Nat. Cancer Inst.*, 1940, **1**, 303; Lacassagne *et al.*, *Compt. rend.*, 1948, **227**, 1119), of the two angular benzacridines (Buu-Hoï, *J.*, 1950, 1146), and in the carbazole series (Buu-Hoï *et al.*, *J. Org. Chem.*, 1951, **16**, 309, 1198; *J.*, 1952, 279) have been investigated; however, no fluorinated molecules in these series have been prepared. Such compounds are of interest, because the physical and chemical properties of the fluorine substituent are closer to those of hydrogen. This finds biological expression in the ability of 4-amino-2-fluorobenzoic acid to antagonise the bacteriostatic activity of sulphanilamide (cf. Sexton, "Chemical Constitution and Biological Activity," Spon, London, 1949, p. 119) and in the antagonistic properties of 3-fluorotyrosine and 3-fluorophenylalanine towards phenylalanine in certain bacteria (Mitchell and Niemann, *J. Amer. Chem. Soc.*, 1947, **60**, 1232).

Synthesis of four fluoro-1 : 2- and -3 : 4-benzacridines is now reported, all bearing a methyl group in 5-position in view of the known favourable effect of *meso*-substitution

* Part XI, *J.*, 1952, 2225.

on carcinogenic activity in this series (cf. Lacassagne, Buu-Hoï, Lecocq, and Rudali, *Bull. Cancer*, 1946, **33**, 48; 1947, **34**, 22; Buu-Hoï and Zajdela, *Acta Unio Intern. contra Cancrum*, 1950, **7**, 184). Condensation of *p*-fluoroaniline with α- and β-naphthol in the presence of iodine was found easily to yield *N*-*p*-fluorophenyl-α- and *N*-*p*-fluorophenyl-β-naphthylamine, whereas in the case of *p*-chloroaniline, similar condensations resulted in partial or complete loss of the halogen (Knoevenagel, *J. pr. Chem.*, 1914, **89**, 17); the modified Bernthsen reaction of these secondary arylamines with acetic anhydride (cf. Buu-Hoï and

(I) 



(II)

Lecocq, *Compt. rend.*, 1944, **218**, 792) gave respectively 7-fluoro-5-methyl-1 : 2- (I) and 7-fluoro-5-methyl-3 : 4-benzacridine (II; R = R′ = H, R″ = F). *o*-Fluoroaniline also underwent condensation with β-naphthol without loss of fluorine, to give *N*-*o*-fluorophenyl-β-naphthylamine, Bernthsen reaction then yielding 9-fluoro-5-methyl-3 : 4-benzacridine (II; R = F, R′ = R″ = H). 7-Fluoro-5 : 8-dimethyl-3 : 4-benzacridine (II; R = H, R′ = Me, R″ = F) was similarly prepared *via* *N*-(4-fluoro-3-methylphenyl)-β-naphthylamine, from 4-fluoro-3-methylaniline. The last-mentioned benzacridine is assigned the 7-fluoro-5 : 8-dimethyl structure in view of the *para*-directing influence of methyl in acridine syntheses, but the alternative 7-fluoro-5 : 8-dimethyl orientation is not excluded. 4-Fluoro-3-methylaniline was synthesised from *o*-fluorotoluene by Friedel–Crafts acetylation, and Beckmann rearrangement of the oxime of the resulting 4-fluoro-3-methylacetophenone; orientation of the entrant acyl radical was inferred from Schiemann's observations (*Ber.*, 1929, **62**, 1797) that, in nitration, the directing effect of the fluorine atom superseded that of the methyl group (cf. the acetylation of *o*-chlorotoluene; Claus, *J. pr. Chem.*, 1891, **43**, 356; 1892, **46**, 26). A more rigid proof of the constitution of our ketone was obtained by its hypobromite oxidation to a fluorotoluic acid which must be 4-fluoro-3-methylbenzoic acid, as it was different from the known 3-fluoro-4-methylbenzoic acid (Paterno and Oliveri, *Gazzetta*, 1882, **12**, 93).

The benzacridines described herein are undergoing biological examination for carcinogenic activity by Professor Lacassagne and Dr. Zajdela, and have shown considerable toxicity.

Experimental

N-p- *and* -o-*Fluorophenyl-α-naphthylamine.*—*p*-Fluoroaniline (10 g.; prepared by reduction of *p*-fluoronitrobenzene), α-naphthol (18 g.), and iodine (0·2 g.) were gently refluxed for 12 hours; the cooled product was taken up in benzene, washed with aqueous sodium hydroxide and with water, dried (Na_2SO_4), freed from solvent, and distilled. N-p-*Fluorophenyl-α-naphthylamine* (11 g.) had b. p. 275—278°/25 mm., and crystallised from methanol as fine colourless prisms, m. p. 91° (Found: C, 80·8; H, 5·1. $C_{16}H_{12}NF$ requires C, 81·0; H, 5·0%). A similar reaction performed with *o*-fluoroaniline (prepared by reduction of *o*-fluoronitrobenzene) gave N-o-*fluorophenyl-α-naphthylamine* (8 g.), forming from methanol silky colourless needles, m. p. 90° (Found: C, 80·7; H, 5·2%).

7-*Fluoro-5-methyl*-1 : 2-*benzacridine.*—*N*-*p*-Fluorophenyl-α-naphthylamine (6 g.), freshly fused zinc chloride (6 g.), and acetic anhydride (6 g.) were heated at 180—185° for 18 hours; after cooling, the mixture was treated with aqueous sodium hydroxide, the insoluble part taken up in toluene, and the toluene solution dried (Na_2SO_4). After removal of the solvent, the residue gave on vacuum-distillation (b. p. >290°/20 mm.) 7-*fluoro-5-methyl*-1 : 2-*benzacridine*, crystallising from ethanol as silky pale yellow needles (3 g.), m. p. 166°, giving an intense greenish-yellow colour with sulphuric acid (Found: C, 82·7; H, 4·5. $C_{18}H_{12}NF$ requires C, 82·8; H, 4·6%). The corresponding *picrate* formed from benzene deep yellow prisms, m. p. 217—218° (decomp. above 200°) (Found: N, 11·2. $C_{24}H_{15}O_7N_4$ requires N, 11·4%).

7-*Fluoro-5-methyl*-3 : 4-*benzacridine.*—Similarly prepared from *N*-*p*-fluorophenyl-β-naphthylamine (Smith, *J. Org. Chem.*, 1951, **16**, 415), this derivative formed from ethanol pale yellow

needles (5 g.), m. p. 177° (Found : C, 82·8; H, 4·8%); its picrate formed from toluene orange-yellow prisms, decomp. above 210°.

N-*o*-*Fluorophenyl*-β-*naphthylamine*.—*o*-Fluoroaniline (10 g.), β-naphthol (10 g.), and iodine (0·2 g.) were refluxed for 8 hours, and worked up in the usual way; the secondary amine obtained (15 g.; b. p. 251—253°/16 mm.) crystallised from methanol as colourless needles, m. p. 82° (Found : C, 81·1; H, 5·2%).

9-*Fluoro*-5-*methyl*-3 : 4-*benzacridine*.—This *fluoro*-compound formed from ethanol fine yellowish needles, m. p. 170—171° (Found : C, 82·7; H, 4·8%); its picrate crystallised from benzene as deep yellow prisms, decomp. above 200°.

4-*Fluoro*-3-*methylacetophenone*.—A solution of *o*-fluorotoluene (30 g.) and acetyl chloride (22 g.) in dry carbon disulphide (150 c.c.) was treated with powdered aluminium chloride (46 g.), and the mixture obtained kept at room temperature for 24 hours and then refluxed for 2 hours. After the usual treatment, the *ketone* was obtained as a colourless liquid, b. p. 214—215° (32 g.; 78%) (Found : C, 71·0; H, 5·9. C_9H_9OF requires C, 71·1; H, 5·9%); the *semicarbazone* crystallised from ethanol as leaflets, m. p. 221° (Found : N, 19·8. $C_{10}H_{12}ON_3F$ requires N, 20·1%), and the *oxime* from ethanol as needles, m. p. 79° (Found : C, 64·4; H, 6·1. $C_9H_{10}ONF$ requires C, 64·7; H, 6·0%).

4-*Fluoro*-3-*methylbenzoic Acid*.—4-Fluoro-3-methylacetophenone (10 g.) was oxidised with ice-cold aqueous sodium hypobromite [made from bromine (22 c.c.) and sodium hydroxide (42 g.)]; the resultant *acid* crystallised from benzene as colourless leaflets, m. p. 168—169° (Found : C, 62·2; H, 4·8. $C_8H_7O_2F$ requires C, 62·3; H, 4·5%); 4-*fluoro*-3-*methylbenzoyl chloride* (2·8 g.), prepared from the acid (4 g.) and thionyl chloride (3·5 g.), was a colourless liquid, b. p. 110—115°/20 mm. (Found : C, 55·2; H, 3·4. C_8H_6OClF requires C, 55·5; H, 3·5%).

4-*Fluoro*-3-*methylaniline*.—A cooled solution of 4-fluoro-3-methylacetophenone oxime (2 g.) in anhydrous ether was treated with finely powdered phosphorus pentachloride (2·1 g.) with shaking; after 5 minutes, the mixture was poured on ice, the ethereal layer collected, washed with aqueous sodium carbonate, dried (Na_2SO_4), and freed from solvent, and the solid residue recrystallised from ether–light petroleum; 4-*fluoro*-3-*methylacetanilide* (1·8 g.) formed colourless leaflets, m. p. 74° (Found : C, 64·6; H, 6·1. $C_9H_{10}ONF$ requires C, 64·7; H, 6·0%). 4-Fluoro-3-methylaniline hydrochloride was prepared by heating this amide for 2 hours with hydrochloric acid; the solid hydrochloride obtained gave on basification 4-*fluoro*-3-*methylaniline*, crystallising from light petroleum as prisms, m. p. 35° (Found : C, 67·0; H, 6·3. C_7H_8NF requires C, 67·2; H, 6·4%); it was best characterised by its condensation product with 2 : 3-dichloro-1 : 4-naphthaquinone : 2-*chloro*-3-(4-*fluoro*-3-*methylanilino*)-1 : 4-*naphthaquinone* crystallised from ethanol as red leaflets, m. p. 216° (Found : C, 64·5; H, 3·8. $C_{17}H_{11}O_2NClF$ requires C, 64·7; H, 3·5%).

N-(4-*Fluoro*-3-*methylphenyl*)-β-*naphthylamine*.—The *amine* crystallised from methanol as colourless leaflets (90% yield), m. p. 83° (Found : N, 5·5. $C_{17}H_{14}NF$ requires N, 5·6%).

7-*Fluoro*-5 : 8-*dimethyl*-3 : 4-*benzacridine*.—This *benzacridine* formed from ethanol pale yellow needles, m. p. 175°, b. p. 290—292°/18 mm. (Found : C, 82·6; H, 5·0. $C_{19}H_{14}NF$ requires C, 82·9; H, 5·1%); its *picrate* crystallised from xylene as deep yellow needles, m. p. 250° (decomp. above 210°) (Found : N, 11·3. $C_{25}H_{17}N_4O_7F$ requires N, 11·6%).

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805. *A General Route to ββ′-Substituted Pyrrole Intermediates for Porphyrin Synthesis.*

By S. F. MacDonald.

New pyrrole intermediates, (VIII*d*) and (X*d*), have been prepared by modifications of standard methods, the essential step being the substitution of benzyl acetoacetate for ethyl acetoacetate in the Knorr syntheses. As already briefly reported (MacDonald, *Chem. and Ind.*, 1951, 759) these should lead to the hitherto unknown pyrroles related to the uroporphyrins, with acetic and propionic acid residues in the ββ′-positions.

A new synthesis of hæmopyrrolecarboxylic acid has been carried out through (X*d*). The ambiguity in its previous syntheses extended to those of the coproporphyrins II and III, and there had consequently been no general method for preparing their homologues.

An earlier alternative solution to these problems had failed when it proved impossible to introduce appropriate β-substituents into the pyrroles by the usual methods. This can be attributed to the effect of α-carbethoxy-groups in diminishing the reactivity of adjacent free β-positions.

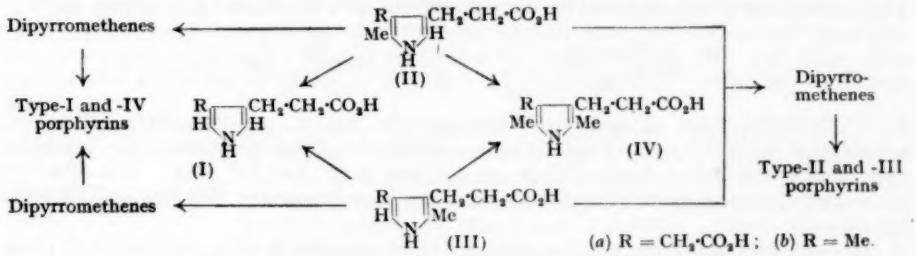
The uroporphyrins were formulated as porphintetra-acetic-tetrapropionic acids by Fischer and Orth ("Chemie des Pyrrols," Leipzig, 1937, Vol. II/i, pp. 504 *et seq.*) and the synthesis of pyrroles with acetic acid and propionic acid residues in the ββ′-positions had consequently been attempted. This was a necessary preliminary to the confirmation of the structures by synthesis, both of these porphyrins and of their oxidation product, a carboxylated hæmatinic acid. Such pyrroles have remained unknown; they could not be isolated from the reduction products of uroporphyrin I, as they did not form picrates (Fischer, *Z. physiol. Chem.*, 1916, **98**, 78; Fischer and Andersag, *Annalen*, 1927, **458**, 117). Were their properties known through synthesis, their isolation should not be difficult.

It was apparent from Fischer's work on analogous porphyrins that all the pyrroles (I*a*), (II*a*), (III*a*), and (IV*a*), and their α-carbethoxy-derivatives, had some importance, either for synthetic work or as probable reduction products of the uroporphyrins. However, the general question of applying his methods systematically to the synthesis of any such set of pyrroles and porphyrins was confused. This was largely because ambiguous reactions had sometimes been used in the syntheses of analogous sets, either for convenience or of necessity, and this obscured the question of their generality. Such reactions also implied indirect methods and proofs of structure which would involve greater difficulties in the present case.

A survey of the extensive literature showed that pyrroles can only be converted unambiguously into pure porphyrins by the routes indicated in Scheme 1. Here, as in Scheme 2, the α-carbethoxy-groups which are necessary for some transformations of the pyrroles are ignored for simplicity. Only those porphyrin syntheses are considered which proceed through dipyrromethenes; the other syntheses cannot be relied on to give porphyrins which are unmixed in type (Fischer, *Ber.*, 1927, **60**, 2649). As indicated in Scheme 1, type-I and type-IV porphyrins can be obtained unambiguously from either of the pyroles (II) and (III) (Fischer and Orth, *op. cit.*, p. 193, methods *b* and *a*; p. 202, "preparation" and method *a*). However, unambiguous methods for preparing pure type-II and type-III porphyrins require both the pyrroles (II) and (III) (Fischer and Andersag, *loc. cit.*; Fischer and Lamatasch, *Annalen*, 1928, **462**, 240; Fischer and Orth, *op. cit.*, p. 200, methods *c* and *b*; the second of the two coproporphyrin II syntheses employs a 5 : 5′-dibromopyrromethene obtained from (I*b*), rather than unambiguously from (II*b*) through the dipyrrylmethane of Fischer and Csukas, *Annalen*, 1934, **508**, 167). These methods avoid the ambiguity introduced by the use of (I) or the aldehyde obtained from it in dipyrromethene synthesis. The four other syntheses of type-II and type-III porphyrins used or implied by Fischer, would also require both the pyrroles (II) and (III) for unambiguous syntheses of the necessary dipyrromethenes.

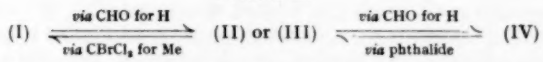
Scheme 1 also indicates the most direct and general method of obtaining all four pyrroles of a set, using the interconversions developed by Fischer (Scheme 2) (Fischer and Orth, *op. cit.*, Vol. I, p. 47 *et seq.*, 278 *et seq.*). Generally, independent syntheses of the key

Scheme 1.



pyrroles (II) and (III) are necessary; their mutual interconversions through the *symmetrical* intermediates (I) and (IV) will not always be possible, and the direction in which interconversion is possible cannot be predicted.

Scheme 2.



More direct syntheses of the symmetrical (I) and (IV) have no advantage when (II) or (III) is available, and their usefulness is limited as discussed above. When carbethoxy-groups are used to block the α-positions, more direct syntheses of (I) will be very restricted; the effect of these groups is discussed below. Direct syntheses of (IV), where no such blocking is required, should be most general. Though little developed, the steps here have been indicated (Fischer and Orth, *op. cit.*, Vol. I, pp. 155, 164, 263, 287, 289), but the removal of a methyl group to free an α-position requires conditions inappropriate when easily decarboxylated acetic acid side-chains are present as in (IV*a*) (Scheme 2).

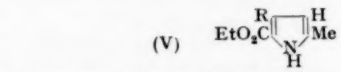
It was apparent that independent syntheses of (II*a*) and (III*a*) would have to be found; only thus could straightforward syntheses of all the required pyrroles and uroporphyrins be projected according to Fischer's methods. The known methods were inadequate.

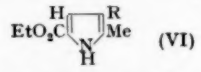
The same problem in pyrrole synthesis had arisen in connection with the coproporphyrins, but had received no general solution. The material (III*b*), the coproporphyrins I and IV, and homologues of these are available by general methods. However, the synthesis of hæmopyrrolecarboxylic acid (II*b*) (Fischer and Treibs, *Ber.*, 1927, **60**, 377), and consequently those of authentic coproporphyrins II and III, depended on the fortunate course of ambiguous reactions involving (I*b*) or (IV*b*); authentic homologues of these are unknown.

General methods had led to all the purely alkyl analogues of (II) and (III) and to all the ætioporphyrins and their homologues. Here, the convenient but unnecessary use of the α-aldehyde obtained from 3-ethyl-4-methylpyrrole has led to confusion; its structure is still in doubt (Fischer, Baumann, and Riedl, *Annalen*, 1930, **475**, 240; Siedel, *Z. physiol. Chem.*, 1935, **231**, 186; Fischer and Hoefelmann, *ibid.*, 1938, **251**, 187; Siedel and Winkler, *Annalen*, 1943, **554**, 169).

One obvious approach to (II*a*), (III*a*), (II*b*), and homologues of the last, was to introduce the second β-substituent into (V; R = $CH_2{\cdot}CO_2H$ or R = $CH_2{\cdot}CH_2{\cdot}CO_2H$), for (V; R = alkyl) had thus been the only important primary source of pyrrole- and porphin-propionic acids. However, the required intermediates could not be prepared by available methods. Numerous attempts had therefore been made to introduce the second substituent into (VI) which, unlike (V), could be obtained without restriction on R. These failed because of the unrecognized effect of an α-carbethoxy-group in blocking the adjacent β-position to substitution by the Gattermann–Hoesch reaction or by use of $MeO{\cdot}CH_2{\cdot}CH(CO_2Et)_2$, the

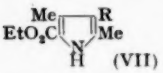
reactions through which $CH_2{\cdot}CH_2{\cdot}CO_2H$ and $CH_2{\cdot}CO_2H$ had been introduced into (V; R = alkyl). Thus (VI; R = Me or $CH_2{\cdot}CH_2{\cdot}CO_2H$) (Fischer and Hussong, *Annalen*, 1932, **492**, 141; Fischer and Kutscher, *ibid.*, 1930, **481**, 193) had failed to give aldehydes leading to (II*b*) or (III*a*), and (VI; R = CN or CO_2Et) (Fischer and Hussong, *loc. cit.*; Fischer and Elhardt, *Z. physiol. Chem.*, 1939, **257**, 61) was likewise unreactive. The description of the 4-glyoxylic ester derivative of (VI; R = CHO) refers to [VI;



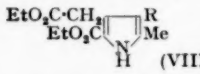


R = $CH{:}C(CN){\cdot}CO_2Et$] (Fischer and Orth, *op. cit.*, Vol. I, pp. 228, 308). However, substitution in (VI) by the Friedel–Crafts method and its condensation with formaldehyde is still possible (Fischer and Orth, *op. cit.*, Vol. I, pp. 192, 197, 348). The effect of an α-cyano-group in preventing substitution had been recognized (Fischer and Elhardt, *loc. cit.*).

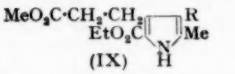
The necessary reactivity was therefore not to be expected in (VI), and that in (V) was uncertain. Although (V; R = alkyl) had given aldehydes and glyoxylic esters and reacted with $MeO{\cdot}CH_2{\cdot}CH(CO_2Et)_2$ (Fischer and Orth, *op. cit.*, Vol. I, pp. 163, 165, 293, 295, 308), the only example of interest here (V; R = $CH_2{\cdot}CN$) had not (Fischer and Elhardt, *loc. cit.*; Fischer and Mueller, *Z. physiol. Chem.*, 1937, **246**, 31). However, the only route to (II*a*), (III*a*), and the homologues of (II*b*) by these methods lay in the assumption that (V) generally would show the desired reactivity, (V; R = $CH_2{\cdot}CN$) being incorrectly formulated. This finds some justification, as it had failed to give the pine-splint and Ehrlich reactions (Fischer and Mueller, *loc. cit.*; Benary, *Ber.*, 1919, **53**, 2218), in contrast to (V; R = alkyl) (see below), and its mode of formation was obscure.



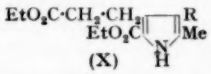
(*a*; R = CO_2Et)
(*b*; R = $CO_2{\cdot}CH_2Ph$)
(*c*; R = CO_2H)
(*d*; R = H)
(*e*; R = COCl)
(*f*; R = $CO{\cdot}NH{\cdot}NH_2$)
(*g*; R = $CH_2{\cdot}NMe_2$)



(a; R = CO_2Et)
(*b*; R = $CO_2{\cdot}CH_2Ph$)
(*c*; R = CO_2H)
(*d*; R = H)
[*e*; R = $CH_2{\cdot}CH(CO_2Et)_2$]
(*f*; R = CHO)



(*a*; R = CO_2Et)
(*b*; R = $CO_2{\cdot}CH_2Ph$)
(*c*; R = CO_2H)
(*d*; R = H)



(*b*; R = $CO_2{\cdot}CH_2Ph$)
(*c*; R = CO_2H)
(*d*; R = H)
(*e*; R = CHO)

The most direct route to (V; R = alkyl) is typified by the condensation of oximinoacetoacetic ester and acetoacetic ester to (VII*a*) (Knorr), its partial hydrolysis in concentrated sulphuric acid at 40° to (VII*c*), and decarboxylation to (VII*d*) (Fischer and Wallach, *Ber.*, 1925, **58**, 2820; Fischer and Orth, *op. cit.* Vol. I, p. 239; cf. *Org. Synth.*, Coll. Vol. II, p. 198). Similarly, oximinoacetonedicarboxylic ester and β-keto-α-oximinoadipic ester with acetoacetic ester gave (VIII*a*) (Fischer and Mueller, *loc. cit.*; Fischer Neumann, and Hirschbeck, *Z. physiol. Chem.*, 1943, **279**, 1) and (IX*a*) (this paper; Professor A. Treibs, personal communication) respectively, but these did not thus yield (VIII*d*) or (IX*d*). The substitution of the readily available benzyl acetoacetate (Bacon, *Amer. Chem. J.*, 1905, **33**, 79) for ethyl acetoacetate in the Knorr syntheses has led to a sufficiently general synthesis of (V). Thus (VII*b*), (VIII*b*), (IX*b*), and (X*b*) were prepared, hydrogenated to (VII*c*), (VIII*c*), (IX*c*), and (X*c*), and decarboxylated to (VII*d*), (VIII*d*), (IX*d*), and (X*d*).

The substance (VII*b*) was used to explore the reaction, for it gave the known pyrroles (VII*c*) and (VII*d*) which are better prepared from (VII*a*).

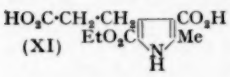
The structure of (VIII*d*) was confirmed by its hydrolysis to (V; R = $CH_2{\cdot}CO_2H$) followed by decarboxylation to the known (VII*d*); its reactivity is illustrated by the formation of (VIII*e*) with $MeO{\cdot}CH_2{\cdot}CH(CO_2Et)_2$, and further by formation of (VIII*f*) by the Gattermann-Hoesch method (MacDonald, *loc. cit.*), leading to transformations completely establishing its structure, and to (III*a*).

The benzyl ester (X*b*) has been a preferred alternative to (IX*b*), because it can be prepared

from a more reliable β-ketoadipic ester, obtained from the crystalline acid (Eisner, Elvidge, and Linstead, *J.*, 1950, 2226). The pyrrole (X*d*) also proved reactive, giving the aldehyde (X*e*), the structure of which was confirmed by Wolff–Kishner reduction to hæmopyrrolecarboxylic acid (II*b*), previously synthesised by Fischer and Treibs (*loc. cit.*). The conversion of (X*d*) into (II*a*) is being studied.

This synthesis of hæmopyrrolecarboxylic acid makes Fischer's syntheses of the coproporphyrins II and III unambiguous throughout, and the same methods should now give the homologues of these (cf. Fischer and Stangler, *Annalen*, 1928, **462**, 253, 261). The pyrrole (X*d*) also provides a route to (II; R = CH_2·CH_2·CO_2H) and porphinoctapropionic acid.

After (IX*c*) had been precipitated by carbon dioxide from an alkaline solution of the crude product (see below), sulphur dioxide precipitated much (XI) which had remained in solution. Decarboxylation of (XI) gave (V; R = CH_2·CH_2·CO_2H), the structure of which was confirmed by comparison with the same product obtained by the alkaline hydrolysis of (X*d*); it gave (X*d*) in good yield on esterification. (XI) also arose as a by-product in the preparation of (X*c*). Fortunately, the acetic ester group in (VIII*c*) is more resistant to hydrolysis, for the free acetic acid group, unlike the propionic acid group would not survive the subsequent decarboxylation.



(XI)

All these pyrroles give a positive Ehrlich's reaction, those of the series (VIII), (IX), and (X) behaving like the analogous members of the series (VII). It is interesting that (VI; R = Me or CH_2·CH_2·CO_2H) do not give a positive Ehrlich's reaction in the cold (Fischer and Hussong, *loc. cit.*; Fischer and Fink, *Z. physiol. Chem.*, 1948, **283**, 152); the more reactive isomers (V; R = Me or CH_2·CH_2·CO_2H) do. The behaviour of the alleged (V; R = CH_2·CN) remains unexplained; an approach to such a structure is being made through (V; R = CH_2·CO·NH_2) obtained from (VIII*d*).

Standard conditions were found for the Knorr syntheses, the formation of the half-esters, and for their purification and decarboxylation. The Knorr syntheses were carried out at 60° (cf. Fischer and Orth, *op. cit.*, Vol. I, pp. 257, 258), the oximino-ester and zinc dust being added to the other components (Corwin and Quattlebaum, *J. Amer. Chem. Soc.*, 1936, **58**, 1081). The catalytic debenzylations were carried out over Raney nickel in dried ethanol, at 100°/100 atm. as the pyrroles were not easily soluble. These acids, (VII*c*), (VIII*c*), (IX*c*), and (X*c*), were insoluble in aqueous sodium hydrogen carbonate. They were purified by precipitation from cold dilute solutions of their sodium salts, by use of carbon dioxide instead of acid; the products were then much more easily filtered and were free from mineral acid. 3-Carbethoxy-2 : 4-dimethylpyrrole-5-carboxylic acid, the isomer of (VII*c*), is also insoluble in bicarbonate, but free propionic and acetic acids derived from (VIII), etc., are soluble in it. None of the published methods gave consistent results when applied to the decarboxylation of these acids to (VII*d*), (VIII*d*), (IX*d*), and (X*d*). Too little or too much heating results in incomplete decarboxylation or in extensive decomposition; the cessation of frothing is no guide here, even in the case of (VII*c*). It is probable that the thermal formation and decomposition of dimers complicates the reactions, and unchanged acids, particularly (VII*c*), may sublime to contaminate distilled products. It was found that heating to 230° in glycerol, followed as rapidly as foaming permitted by steam-distillation at 280° (steam not preheated), gave consistently maximal yields of products which crystallized directly in the receiver, high-melting impurities being then absent.

Much the best method of preparing (VII*d*) is that of Fischer and Wallach (*loc. cit.*) through (VII*a*) (see above). With these modifications in the Knorr synthesis of (VII*a*) and in the purification and decarboxylation of (VII*c*), pure (VII*d*) was obtained in 45% yield from ethyl acetoacetate. It was thought that the partial hydrolysis of (VII*a*) to (VII*c*) in concentrated sulphuric acid might be analogous to that of mesitoic esters (Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1708), but (VII*a*) was recovered unchanged after treatment with 100% sulphuric acid at 10°.

Some experiments were begun on further methods for introducing acetic acid and propionic acid groups into (VII*d*). With carbonyl chloride (cf. Fischer and Orth, *op. cit.*, Vol. I, p. 313) it gave (VII*e*), identified by conversion into (VII*a*), and it also readily gave

the Mannich base (VII*g*) (cf. Fischer and Nenitzescu, *Annalen*, 1925, **443**, 113). It did not react with cyanoacetic ester under Gattermann–Hoesch conditions (cf. Fischer and Orth, *op. cit.*, Vol. I, p. 310). An attractive alternative to decarboxylating (VII*c*) and its analogues was to utilize the carboxyl group to build up the side-chain, a method which should also be applicable in pyrroles where the free β-position would be inactivated by an adjacent α-carbethoxy-group (see above). Acetyl chloride converted (VII*c*) into the acid chloride (VII*e*), which gave (VII*a*) and (VII*f*) with ethanol and hydrazine respectively.

Experimental

M. p.s are uncorrected.

Diethyl 3 : 5-*Dimethylpyrrole*-2 : 4-*dicarboxylate* (VII*a*).—Acetoacetic ester (400 g.) in acetic acid (900 c.c.) was treated slowly with sodium nitrite (220 g.) in water (300 c.c.) at 4—7°, and the resulting solution run into a stirred mixture of acetoacetic ester (400 g.), acetic acid (1400 c.c.), and zinc dust (600 g.) in a 5-l. flask cooled in water. The addition wsa made at 60°, rising to 100°, to keep the product in solution; stirring at 100° was then continued 1·5 hours. The product was isolated as usual (Fischer and Orth, *op. cit.*, Vol. I, p. 255), giving 536 g. (73%) of vacuum-dried ester.

Benzyl 5-*Carbethoxy*-2 : 4-*dimethylpyrrole*-3-*carboxylate* (VII*b*).—Sodium nitrite (13·8 g.) in water (20 c.c.) was slowly added with stirring to ethyl acetoacetate (26 g.) in acetic acid (100 c.c.) at 4—8°. After 15 minutes, benzyl acetoacetate (38·4 g.) and anhydrous sodium acetate (25 g.) were added, followed by a mixture of zinc dust (35 g.) and sodium acetate (10 g.) during 30 minutes. To keep the product in solution, acetic acid (100 c.c.) was added, and the mixture allowed to boil. The mixture was refluxed for 1 hour and decanted from zinc into water. The *product* was filtered off and washed with water, giving 35 g. (58%), m. p. 140—145°. For analysis, it was crystallized from ethanol, distilled (150—170°/5 × 10^{-3} mm.), and recrystallized several times, forming colourless plates, m. p. 151—151·5° (Found: C, 67·3; H, 6·3; N, 4·8. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4; N, 4·6%). Ehrlich's reaction weakly positive in the hot.

5-*Carbethoxy*-2 : 4-*dimethylpyrrole*-3-*carboxylic Acid* (VII*c*).—(*a*) *By Fischer and Wallach's method* (loc. cit.). The crude diethyl ester (VII*a*) was treated with sulphuric acid and poured on ice. The precipitate was filtered off (cloth filter) and washed with water (500 c.c.; thorough washing is difficult and unnecessary). It was stirred in water (1 l.) for 30 minutes, 10% aqueous sodium hydroxide being added to alkalinity (phenolphthalein). The filtered solution was made up to 2·5 l. with ice and water and saturated with carbon dioxide; the product (67·6 g., 77%) was filtered off, washed with water, and vacuum-dried. When the diester (VII*a*) (100 g.) was treated with sulphuric acid (200 c.c.) at 10° and 20% oleum (200 c.c.) was added at 10°, the diester (95 g.) was recovered unchanged.

(*b*) *From benzyl* 5-*carbethoxy*-2 : 4-*dimethylpyrrole*-3-*carboxylate* (VII*b*). The benzyl ester (5 g.) was hydrogenated for 4 hours (50°/100 atm.) in ethanol (250 c.c.) with Raney nickel (7 g.). After filtration and removal of the solvent, the product was dissolved in dilute sodium hydroxide, precipitated with acid, and crystallized from ethanol, forming colourless plates (74%), m. p. 272° (lit., 273°) (Found: C, 56·6; H, 6·35; N, 6·6. Calc. for $C_{10}H_{13}O_4N$: C, 56·85; H, 6·2; N, 6·6%).

Ethyl 3 : 5-*Dimethylpyrrole*-2-*carboxylate* (VII*d*).—(*a*) The acid (VII*c*), from the benzyl ester (VII*b*), was decarboxylated by heating it over a free flame. The product was extracted from the melt with cold ethanol, crystallized from 50% ethanol, and distilled at 200°/30 mm. It had m. p. and mixed m. p. with authentic material 123—124° (Found: C, 64·6; H, 8·0; N, 8·6. Calc. for $C_9H_{13}O_2N$: C, 64·7; H, 7·8; N, 8·4%).

(*b*) *Preparative method.* The acid (VII*d*) (20 g.) was wetted with glycerol (50 g.) in a ½-l. flask with a short wide neck. The mixture was heated at 220—230° until the paste had liquefied, and two further 20-g. portions of the acid were added successively, the heating being repeated after each addition. The contents were then steam-distilled (260—300°, thermometer in mixture) until the distillate became dark and free from oil. The product was filtered off from the distillate, washed with water, crystallized from 95% ethanol (75 c.c.), and washed with ethanol (25 c.c.), giving 40·1 g. of m. p. 123°. The mother-liquiors yielded a further 1·6 g., m. p. 121—122° (total 87%).

5-*Carbethoxy*-2 : 4-*dimethylpyrrole*-3-*carbonyl Chloride* (VII*e*).—(a) *From* (VII*d*). The pyrrole (1 g.) in toluene (25 c.c.) was saturated with carbonyl chloride at 20° and set aside for 2 days. The crystalline acid chloride was filtered off and dried *in vacuo*. Boiling ethanol converted it

into the diester (VII*a*), m. p. 134° undepressed when mixed with an authentic specimen (Found : C, 60·2; H, 7·35; N, 5·9. Calc. for $C_{12}H_{17}O_4N$: C, 60·2; H, 7·2; N, 5·9%).

(b) *From* (VII*c*). The half-ester (1 g.) was refluxed with acetyl chloride (40 c.c.) for 1 hour, then cooled, and the product (0·98 g.) filtered off; the *acid chloride* formed colourless needles, m. p. 203° (Found : C, 52·6; H, 4·8; N, 6·2; Cl, 14·4. $C_{10}H_{12}O_3NCl$ requires C, 52·3; H, 5·3 N, 6·1; Cl, 15·4%). Boiling ethanol converted it into the diester (VII*a*), m. p. 134—134·5°.

5-Carbethoxy-2 : 4-dimethylpyrrole-3-carboxyhydrazide (VII*f*).—The acid chloride (VII*g*) (0·98 g.) was dissolved in dioxan (10 c.c.) containing hydrazine hydrate (100%; 2 c.c.) at 0°. The *product* was precipitated with water, filtered off, dissolved in dilute acid, and re-precipitated with alkali, yielding needles (from ethanol), m. p. 220° (Found : C, 53·1; H, 6·9; N, 18·6. $C_{10}H_{15}O_3N_3$ requires C, 53·3; H, 6·7; N, 18·65%).

Ethyl 3 : 5-Dimethyl-4-dimethylaminomethylpyrrole-3-carboxylate (VII*g*).—The pyrrole (VII*d*) (16·7 g.) was heated under reflux for 3 hours with ethanol (50 c.c.), dimethylamine hydrochloride (10 g.), and 40% formaldehyde solution (10 g.). After concentration, addition of water (250 c.c.), and filtration warm, the *product* (21 g., 94%) was precipitated with aqueous sodium hydroxide. It was purified by precipitation as the hydrochloride from ethanol, and the regenerated base crystallized from 40% ethanol as colourless long plates, m. p. 121° (Found : C, 63·9; H, 8·85; N, 12·6. $C_{12}H_{20}O_2N_2$ requires C, 64·3; H, 9·0; N, 12·5%). Ehrlich's reaction was positive in the hot.

Benzyl 5-Carbethoxy-4-carbethoxymethyl-2-methylpyrrole-3-carboxylate (VIII*b*).—Amyl nitrite (117 g.; twice distilled) was added during 1 hour at 20° to a stirred and cooled mixture of ethyl acetonedicarboxylate (*Org. Synth.*, Coll. Vol. I, 2nd edn., p. 237) and concentrated hydrochloric acid (1·5 c.c.). After the addition, the temperature was allowed to rise spontaneously to 25°; the mixture was then heated to 40° and set aside at room temperature overnight. It was then run during 40 minutes into a vigorously stirred mixture of ammonium acetate (150 g.), acetic acid (1 l.), benzyl acetoacetate (192 g.), and zinc dust (50 g.) in a 2-l. flask cooled in ice-water. During the addition, zinc dust (100 g.) was added in small portions and the temperature was kept at 60—65°. The cooling-bath was then removed and, after the temperature rise ceased, the mixture was slowly heated to 95° during 2 hours, stirring being continued. The hot solution was decanted from zinc into well-stirred ice-water (12 l.), and the zinc washed with hot 50% acetic acid. The *product* was filtered off after 2 hours, washed with 50% ethanol (500 c.c.), and crystallized from absolute alcohol (280 c.c.) (charcoal), giving 203·5 g. (55%) of m. p. 120—123°; after several recrystallizations it formed colourless flat prisms, m. p. 123—124° (Found : C, 64·5; H, 6·2; N, 3·8. $C_{20}H_{23}O_6N$ requires C, 64·3; H, 6·2; N, 3·8%). Ehrlich's reaction was positive in the hot.

Inferior ethyl acetonedicarboxylate gives once-recrystallized products which begin to melt at about 110°; they are quite satisfactory for the subsequent stages. Use of sodium nitrite and acetic acid in place of amyl nitrite lowered the yield considerably (cf. Fischer and Mueller, *loc. cit.*; Fischer, Neumann and Hirschbeck, *loc. cit.*).

5-Carbethoxy-4-carbethoxymethyl-2-methylpyrrole-3-carboxylic Acid (VIII*c*).—The benzyl ester (VIII*b*) (70 g.) was hydrogenated in absolute ethanol (800 c.c.) over Raney nickel (5 c.c.) for 3 hours at 100°/100 atm. The bulk of the product was filtered off and more obtained by evaporation of the ethanol. Three such lots (from 203 g. of benzyl ester) were combined, dissolved in cold aqueous sodium hydroxide, diluted to 0·1M (*ca.* 6 l.), filtered, and saturated with carbon dioxide at 0°. The precipitated *product* was filtered off, washed with water (3 l.), and dried at 100°, giving 139·5 g. (91%) of m. p. 238—239° (decomp.). After three recrystallizations from acetic acid, colourless prisms, m. p. 240° (decomp.), were obtained, which give Ehrlich's reaction very faintly in the hot (Found : C, 55·5; H, 6·2; N, 5·1. $C_{13}H_{17}O_6N$ requires C, 55·1; H, 6·05; N, 4·9%).

Batches of 125 g. were hydrogenated at 125°/150 atm. but with no increase in the amount of ethanol or nickel.

Ethyl 3-Carbethoxymethyl-5-methylpyrrole-2-carboxylate (VIII*d*).—The above carboxylic acid (15 g.) was wetted with glycerol (45 g.) in a ½-l. bolt-head flask fitted with a steam-inlet and a thermometer reaching to the bottom and with a downward air-condenser leading to a Liebig condenser. The mixture was heated with a moving free flame to 230° until foaming ceased. The temperature was then rapidly raised to 270—280° and a current of steam (not superheated) passed in until the distillate was highly coloured. After cooling and dilution with water, the *product* was filtered off from the distillates of three such runs and crystallized from light petroleum (200 c.c.; b. p. 80—100°) (charcoal) and then from 40% acetic acid (145 c.c.) (charcoal), giving 15·5 g. (41%) of m. p. 90·5—91°. After recrystallizing from 40% ethanol, colourless

plates, m. p. 91—92°, were obtained, giving Ehrlich's reaction in the cold (Found: C, 60·2; H, 6·9; N, 6·0. $C_{12}H_{17}O_4N$ requires C, 60·2; H, 7·2; N, 5·9%).

Ethyl 3-*Carboxymethyl*-5-*methylpyrrole*-2-*carboxylate* (V; R = CH_2·CO_2H).—The diester (VIII*d*) was heated under reflux with a slight excess of 0·1N-sodium hydroxide to effect solution (about 15 minutes), filtered (charcoal), and acidified at 0°. The *product* was filtered off and recrystallized from water as large needles or (more stable form) plates, and from ether; it had m. p. 157° (Found: C, 57·2; H, 6·6; N, 6·55. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2; N, 6·6%).

Reconversion of the Half-ester (V; R = CH_2·CO_2H) *into the Diester* (VIII*d*).—The half-ester with saturated ethanolic hydrogen chloride (18 hours at 15°) gave the diester; crystallized from 40% acetic acid it had m. p. 91—92°, unchanged when mixed with an authentic specimen.

Decarboxylation of the Half-ester (V; R = CH_2·CO_2H) *to Ethyl* 3 : 5-*Dimethylpyrrole*-2-*carboxylate* (VII*d*).—The half-ester was refluxed for 3 minutes with a little resorcinol and poured into water. The precipitated ethyl 3 : 5-dimethylpyrrole-2-carboxylate, crystallized from ethanol, had m. p. 122—123°, unchanged when mixed with an authentic specimen.

Ethyl 3-*Carbamylmethyl*-5-*methylpyrrole*-2-*carboxylate* (V; R = CH_2·CO·NH_2).—The ester (VIII*d*) was set aside in concentrated aqueous ammonia (15 parts) for 10 days. The *product* was filtered off, washed with hot light petroleum (b. p. 80—100°), crystallized from water (200 parts) (charcoal), then from acetone, forming colourless needles, m. p. 205° (Found: C, 57·2; H, 7·0; N, 13·1. $C_{10}H_{14}O_3N_2$ requires C, 57·1; H, 6·7; N, 13·3%). Ehrlich's reaction was positive in the cold.

Ethyl 3-*Carbethoxymethyl*-3-(2 : 2-*dicarbethoxyethyl*)-5-*methylpyrrole*-2-*carboxylate* (VIII*f*).—The pyrrole (VIII*d*) (1·08 g.) was heated under reflux for 1 hour with methoxymethylmalonic ester (1·5 c.c.), ethanol (3 c.c.), and ethanolic hydrogen chloride (saturated at 0°; 1·5 c.c.). After cooling, the solution was poured into ice-water, and the oil separated and left to crystallize in a vacuum-desiccator over potassium hydroxide. The well-crystallized *product* (1·24 g.) remained after draining on tile; twice crystallized from light petroleum (b. p. 40—60°), it formed colourless needles, m. p. 58°, and did not give Ehrlich's reaction in the cold but did so strongly in the hot (Found: C, 58·0; H, 7·3; N, 3·6. $C_{20}H_{29}O_8N$ requires C, 58·4; H, 7·1; N, 3·4%).

Diethyl 4-2′-*Carbomethoxyethyl*-2-*methylpyrrole*-3 : 5-*dicarboxylate* (IX*a*).—Sodium nitrite (0·35 g.) in a little water was added with stirring during 15 minutes to methyl δ-carbethoxylævulate (1 g.) in acetic acid (3 c.c.) at 4°. After ½ hour, ethyl acetoacetate (0·65 c.c.) was added. Anhydrous sodium acetate (2 g.) and zinc dust (2·5 g.) were then added with stirring during 15 minutes at 20—65°. After ½ hour's stirring at 95°, the solution was decanted from the zinc into water, and the zinc washed with hot 50% acetic acid. The *product* was filtered off, washed with water, and crystallized from ethanol (30 c.c. of 33%), giving 1 g. (64%) as colourless needles, m. p. 103—103·5° unchanged on recrystallization (Found: C, 58·3; H, 7·1; N, 4·7. $C_{15}H_{21}O_6N$ requires C, 57·9; H, 6·8; N, 4·5%). Ehrlich's reaction was weakly positive in the hot.

Benzyl 5-*Carbethoxy*-4-2′-*carbomethoxyethyl*-2-*methylpyrrole*-3-*carboxylate* (IX*b*).—Sodium nitrite (3 g.), in water (4 c.c.) was added at 0° to a stirred mixture of methyl δ-carbethoxylævulate (8·4 g.), acetic acid (30 c.c.), and water (1 c.c.). After 1·5 hours at 0°, ammonium sulphamate (1 g.), benzyl acetoacetate (8·5 g.), and acetic acid (20 c.c.) were added. A mixture of zinc dust (8 g.) and anhydrous sodium acetate (8 g.) was gradually added, together with acetic acid (100 c.c.) to the stirred mixture; the temperature rose to 100° and was kept thereat for ½ hour more. The *product* was isolated by pouring the mixture into water, etc., and had m. p. 168—169° (10·2 g., 66%). Twice crystallized from ethanol (500 c.c.) it formed pale yellow plates, m. p. 172° (Ehrlich's reaction positive in the hot) (Found: C, 64·1; H, 6·2; N, 3·9. $C_{20}H_{23}O_6N$ requires C, 64·3; H, 6·2; N. 3·8%).

5-*Carbethoxy*-4-2′-*carbomethoxyethyl*-2-*methylpyrrole*-3-*carboxylic Acid* (IX*c*).—The benzyl ester (6·4 g.) was hydrogenated in ethanol (350 c.c.) over Raney nickel (2 c.c.) for 5 hours at 100°/75 atm. The *product* (3 g.) was obtained as usual by precipitation from dilute aqueous sodium hydroxide with carbon dioxide and crystallized from acetone as colourless plates, m. p. 220° (Ehrlich's reaction positive in the hot) (Found: C, 55·1; H, 5·7; N, 5·2. $C_{13}H_{17}O_6N$ requires C, 55·1; H, 6·0; N, 4·9%).

Ethyl 4-2′-*Carbomethoxyethyl*-5-*methylpyrrole*-2-*carboxylate* (IX*d*).—The acid (IX*c*) (100 mg.) was sublimed at 235°/15 mm., and the *product* extracted with pentane, in which high-melting impurities are less soluble. After distilling at 110°/15 mm., it melted at 65—65·5° (Ehrlich's reaction positive in the cold) (Found: C, 60·5; H, 7·4; N, 5·85. $C_{12}H_{17}O_4N$ requires C, 60·2; H, 7·2; N, 5·9%).

5-*Carbethoxy*-4-2′-*carboxyethyl*-2-*methylpyrrole*-3-*carboxylic Acid* (XI).—The aqueous alkal-

ine mother-liquor from (IX*c*) was acidified with sulphur dioxide; the *product* (2·2 g.) formed small colourless needles, m. p. 253° (decomp.), from acetic acid (Found: C, 53·6; H, 5·5; N, 5·4. $C_{12}H_{15}O_6N$ requires C, 53·5; H, 5·6; N, 5·2%).

Ethyl 3-2′-*Carboxyethyl*-5-*methylpyrrole*-2-*carboxylate* (V; R = CH_2·CH_2·CO_2H).—The crude acid (XI) was sublimed at 235°/20 mm. and the *product* purified by washing it with hot light petroleum (b. p. 80—100°), and crystallized from aqueous ethanol; it was dissolved in alkali, precipitated with acid, and crystallized from ether (thimble), forming colourless needles, m. p. 152° alone or mixed with the product obtained from (X*d*) (see below) (Found: C, 58·8; H, 6·9; N, 6·2. $C_{11}H_{15}O_4N$ requires C, 58·6; H, 6·7; N, 6·2%).

Ethyl β-*Ketoadipate*.—β-Ketoadipic acid (Eisner, Elvidge, and Linstead, *loc. cit.*) gave the ethyl ester (70%) by the method given for the esterification of acetonedicarboxylic acid (*Org. Synth., loc. cit.*).

Benzyl 5-*Carbethoxy*-4-2′-*carbethoxyethyl*-2-*methylpyrrole*-3-*carboxylate* (X*b*).—Amyl nitrite (30 g.; twice distilled) was added during 1 hour at 20—25° to ethyl β-ketoadipate (55·5 g.) containing concentrated hydrochloric acid (0·7 c.c.); the temperature was then allowed to rise spontaneously to 40°. Next day the mixture was run into a stirred and cooled mixture of benzyl acetoacetate (50 g.), acetic acid (250 c.c.), zinc dust (15 g.), and ammonium acetate (40 g.) at 60—65° during 1 hour; at the same time zinc dust (40 g.) was added in small portions. The bath was then removed and the mixture stirred for 3 hours at 75—100°. The solution was decanted into well-stirred ice-water (3 l.), the zinc washed, and the *product* filtered off, washed, and dried; crystallized from ethanol (350 c.c.), it had m. p. 140—142° (67·7 g., 68%). Recrystallized from light petroleum (b. p. 60—80°; thimble) and then from ethanol, it formed colourless plates, m. p. 142—143° (Ehrlich's reaction weakly positive in the hot) (Found: C, 65·15; H, 5·95; N, 3·7. $C_{21}H_{25}O_6N$ requires C, 65·1; H, 6·5; N, 3·6%).

5-*Carbethoxy*-4-2′-*carbethoxyethyl*-2-*methylpyrrole*-3-*carboxylic Acid* (X*c*).—The benzyl ester (X*b*) (65 g.) in dried ethanol (500 c.c.) was heated under reflux with Raney nickel (2·5 c.c.), more nickel added (2·5 c.c.), and the whole hydrogenated at 100°/100 atm. for 5 hours. The residue on evaporation was extracted with 10% aqueous sodium hydroxide (160 c.c., diluted with ice and water to 4 l.); the solution was filtered and saturated with carbon dioxide at 0°. The *product* was filtered off, washed well with water, and dried *in vacuo* [42 g., 84%; m. p. 230° (decomp.)]. Crystallized from acetone (thimble) and dried (90°/2 × 10^{-2} mm.) it formed flat colourless needles, m. p. 230° (decomp.) (Ehrlich's reaction positive in the hot) (Found: C, 57·6; H, 6·6; N, 4·5. $C_{14}H_{19}O_6N$ requires C, 56·6; H, 6·4; N, 4·7%).

Ethyl 3-2′-*Carbethoxyethyl*-5-*methylpyrrole*-2-*carboxylate* (X*d*).—The acid (X*c*) (15 g.) was rapidly heated in glycerol (45 g.), with a free flame to 260° until frothing ceased; then a rapid current of steam was introduced at 280° until there was little oil in the condensate. The *product* was separated from the distillate by filtration, crystallized twice from pentane (thimble), and distilled (110°/5 × 10^{-4} mm.) (m. p. *ca.* 65—67°; yield, 51%). It was separated from granular material and obtained as very large colourless prisms by repeated crystallization from pentane, then having m. p. 66° or mixed with (IX*d*) 61°, Ehrlich's reaction being positive in the cold (Found: C, 61·8; H, 7·35; N, 5·5. $C_{13}H_{19}O_4N$ requires C, 61·6; H, 7·6; N, 5·5%). The apparent difficulty in purification has since been traced to polymorphism; resolidified melts may melt at either 56° or at 69°.

Ethyl 3-2′-*Carboxyethyl*-5-*methylpyrrole*-2-*carboxylate* (V; R = CH_2·CH_2·CO_2H).—The crude ester (X*d*) (1 g.) was stirred for 15 minutes at 100° in 0·5N-sodium hydroxide (10 c.c.), cooled, filtered (charcoal), and acidified (Congo-red) with sulphur dioxide at 0°. The *product* was filtered off and crystallized from water (50 c.c.; charcoal), from ether (thimble) and again from water, forming colourless needles (0·23 g.), m. p. 153° [mixed m. p. with (V; R = CH_2·CO_2H) 140°; Ehrlich's reaction positive in the cold] (Found: C, 58·85; H, 6·8; N, 6·4. $C_{11}H_{15}O_4N$ requires C, 58·6; H, 6·7; N, 6·2%).

5-*Carbethoxy*-4-2′-*carbethoxyethyl*-2-*methylpyrrole*-3-*aldehyde* (X*e*).—A solution of the ester (X*d*) (0·52 g.) in dry ether (1·5 c.c.) and dry chloroform (1·5 c.c.) containing anhydrous hydrogen cyanide (1 c.c.) was cooled in ice-salt, and dry hydrogen chloride passed in for 6 hours. After being kept at 0° overnight, the solvent was removed *in vacuo*, the residue washed with ether and dissolved in water (10 c.c.), and the solution filtered and adjusted to pH 4. The *product* (0·24 g., 41%) soon separated and was filtered off, washed with water, and dried (m. p. 118—120°). Crystallized from water (charcoal), then twice from ether–pentane (thimble), it formed colourless plates, m. p. 122° (Found: C, 59·6; H, 6·9; N, 5·0. $C_{14}H_{19}O_5N$ requires C, 59·8; H, 6·8; N, 5·0%).

Hæmopyrrolecarboxylic Acid (II*b*).—The crude aldehyde (X*e*) (0·24 g.) was heated at 100°

for 1 hour with N-sodium hydroxide (2 c.c.) and filtered. The filtrate was evaporated *in vacuo* and the dry residue heated with hydrazine hydrate (0·5 c.c.) and a solution of sodium (0·1 g.) in ethanol (1·5 c.c.) for 14 hours at 160°. Water (4 c.c.) was added, the ethanol removed at 100°, and the product (0·10 g.) precipitated from the filtered solution by sulphur dioxide at 0°. It was twice crystallized from ether–light petroleum, then once from water (15 parts), and sublimed (115°/5 × 10^{-4} mm.), forming colourless prisms, m. p. 129—130° (lit., 130—131°) (Found: C, 64·7; H, 7·7; N, 8·6. Calc. for $C_9H_{13}O_2N$: C, 64·6; H, 7·8; N, 8·4%). Ehrlich's reaction was positive in the cold.

This acid with ethereal diazomethane gave the methyl ester which, crystallized from ether–light petroleum and distilled at 100° *in vacuo*, had m. p. 54—55° (lit., 57°). This gave a picrate, chocolate brown needles, m. p. 119° (lit., 121—122°).

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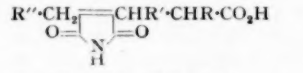
806. *The Syntheses of Pyrroles, a Porphyrin, and the Maleinimide related to the Uroporphyrins.*

By S. F. MACDONALD.

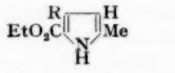
As already briefly reported (MacDonald, *Chem. and Ind.*, 1951, 759, 1092), representatives of the hitherto unknown pyrroles with both acetic acid and propionic acid residues in the β-positions have been synthesized, including one of the hypothetical reduction products of the uroporphyrins. A porphin-tetra-acetic-tetrapropionic acid has been synthesized and oxidized to a carboxylated hæmatinic acid identical with that from natural uroporphyrin I. Though the synthetic porphyrin appears to be a mixture of type isomers, its oxidation and other properties support Fischer's structures for the uroporphyrins.

THE history and chemistry of the uroporphyrins have been summarized by Hans Fischer (*Ber.*, 1927, **60**, 2611; cf. Fischer and Orth, "Chemie des Pyrrols," Leipzig, 1937, Vol. II/i, pp. 504 *et seq.*). As these pigments have no apparent physiological function, general interest in them has depended on the prevailing views on their relation to hæmin. Recently earlier hypotheses have been reversed; the uroporphyrins and the related pyrroles are now postulated as intermediates in the biosynthesis of hæmin (cf. Falk and Rimington, *Ann. Reports*, 1950, 271).

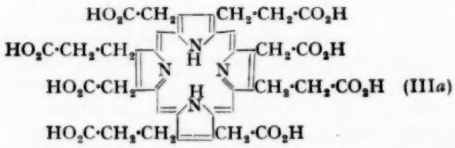
Uroporphyrin I, isolated from the urine of a patient with congenital porphyria, was shown to be an octacarboxylic acid, giving the tetracarboxylic acid coproporphyrin I (III*a*; Me for $CH_2{\cdot}CO_2H$) on partial decarboxylation. Its oxidation gave a carboxylated hæmatinic acid which decarboxylated to hæmatinic acid (I*a*) and to ethylmethylmaleinimide and was formulated as (I*b*, *c*, or *d*).



(I*a*; R = R′ = R″ = H)
(I*b*; R = CO_2H; R′ = R″ = H)
(I*c*; R′ = CO_2H; R = R″ = H)
(I*d*; R″ = CO_2H; R = R′ = H)



(II*a*; R = Me)
(II*b*; R = $CH_2{\cdot}CO_2Et$)
(II*c*; R = $CH_2{\cdot}CH_2{\cdot}CO_2Et$)



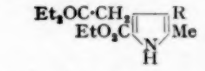
(III*a*)

Pyrroles corresponding to (I*b* and *c*), which could be synthesized from (II*a*), were each converted into the corresponding type-I and type-II porphyrins, tetramethylporphin-tetra(methylmalonic) acids and tetramethylporphintetrasuccinic acids. Neither of the

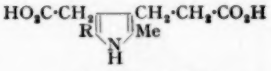
type-I porphyrins was identical with uroporphyrin I. Also, the more available type-II prophyrins were oxidized to the carboxylated hæmatinic acids (I*b* and *c*), which differed from that obtained from uroporphyrin I. Only the structure (I*d*) remained for the analytical carboxylated hæmatinic acid, and Fischer formulated uroporphyrin I as porphin-1 : 3 : 5 : 7-tetra-acetic-2 : 4 : 6 : 8-tetrapropionic acid (III*a*). The other uroporphyrin isomers are formally derived from it by reversing the order of the two β-substituents on two opposite pyrrole nuclei (type II; III*b*), on one pyrrole nucleus (type III; III*c*), or on two adjacent nuclei (type IV; III*d*).

The further development of this approach to the structure and synthesis of the uroporphyrins required the intermediates (II*b* or c) (preceding paper). The transformations of (II*b*) now described are completely analogous to one synthesis of coproporphyrins from (II*a*) (Fischer and Andersag, *Annalen*, 1926, **450**, 201; 1927, **458**, 117).

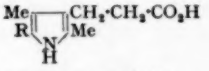
The propionic acid residue was introduced into (IV*a* = II*b*) as usual (Fischer and Orth, *op. cit.*, Vol. I, p. 270) *via* the aldehyde (IV*b*) and the acrylic acid (IV*c*). Catalytic reduction of the last in alkaline solution resulted in partial hydrolysis, and the product was isolated as (V*a*), or better as (IV*d*) after esterification. Hydrolysis of (IV*d*) gave (V*d*), which was stable when dry.



(IV*a*; R = H)
(IV*b*; R = CHO)
(IV*c*; R = CH:CH·CO_2H)
(IV*d*; R = CH_2·CH_2·CO_2Et)
(IV*e*; R = CH_2·CH_2·CO_2Et; CH_2Br for Me)



(V*a*; R = CO_2Et)
(V*b*; R = CO_2H)
(V*c*; R = H)

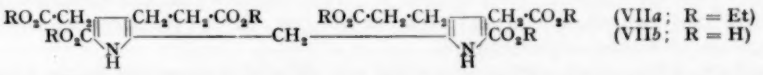


(VI*a*; R = CO_2Et)
(VI*b*; R = CO_2H)
(VI*c*; R = H)

The structures of these pyrroles were confirmed by decarboxylation of the free acetic acids under vigorous conditions to known dimethylpyrroles, as (IV*a*, CH_2·CO_2H for CH_2·CO_2Et) had given ethyl 2 : 4-dimethylpyrrole-5-carboxylate (preceding paper). Thus (V*a*), obtained as above or by the partial hydrolysis of (IV*d*), was decarboxylated to (VI*a*). Similarly, (V*b*) gave (VI*c*). These degradations do not distinguish the relative positions of the methyl and the acetic acid groups. However, the conversion of (IV*d*) into (IV*e*) and thence into the dipyrrylmethane (VII*a*) without the loss of a carbethoxy-group requires a methyl group in the α-position.

Like analogous pyrrole-α-carboxylic acids, (V*b*) was rapidly decarboxylated in water at 100°. The resulting dicarboxylic acid must be (V*c*). In view of the resistance of the propionic acid group to decarboxylation, the only alternative formulation is as the known (VI*b*), which is much less soluble in water and is decarboxylated to (VI*c*) under the above conditions. The acid (V*c*), which might be termed cryptopyrroledicarboxylic acid, is probably one component of the mixture which had been obtained by reducing uroporphyrin I with hydrogen iodide, for extensive decarboxylation did not accompany the reduction (Fischer, *Z. physiol. Chem.*, 1916, **98**, 78; Fischer and Zerweck, *ibid.*, 1924, **137**, 243; Fischer and Andersag, *Annalen*, 1927, **458**, 117). Like the reduction products, (V*c*) is very soluble in water and forms no picrate in wet ether and its methyl ester has been obtained only as an oil. Further work on the characterization of such pyrroles is necessary. With hydrogen iodide and acetic acid at 100°, both (V*b*) and (V*c*) gave high-melting, ether-insoluble products containing iodine (cf. the behaviour of an isomeric pyrrolesuccinic acid, Fischer and Holt, *Z. physiol. Chem.*, 1934, **229**, 94).

With bromine in acetic acid, or better in carbon disulphide, (IV*d*) was converted into (IV*e*), obtained as an oil. In boiling ethanol or water, the latter yielded (VII*a*) which gave (VII*b*) on alkaline hydrolysis.

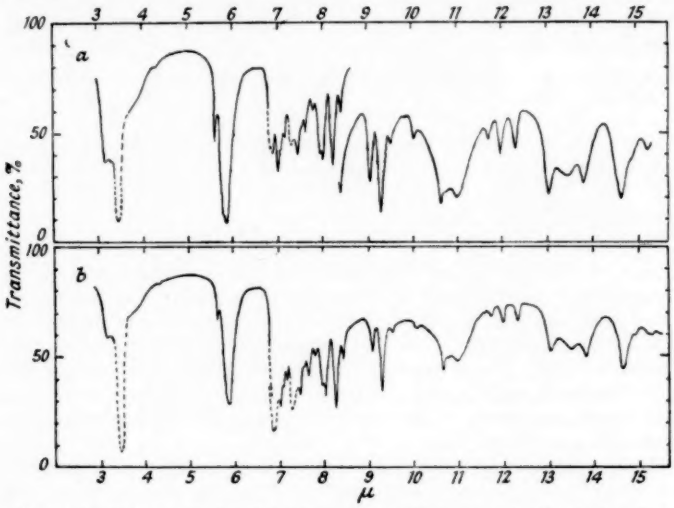


(VII*a*; R = Et)
(VII*b*; R = H)

Although the free acetic acids are sufficiently resistant to decarboxylation, these reactions have been carried out with their ethyl esters because (IV*b*; CH_2·CO_2H for

$CH_2 \cdot CO_2Et$) was inconveniently soluble in water. It is unlikely that this choice was always appropriate. Working with the α-carbethoxy-derivatives of the free propionic or acetic acids would avoid difficulties in handling their esters, which easily undergo hydrolysis and trans-esterification and frequently have low melting points and high solubilities in organic solvents; α-carbethoxy-groups are not inconvenient in these respects.

Prolonged treatment with formic acid at 40° converted (VII*b*) into a porphintetra-acetic-tetrapropionic acid, isolated as the methyl ester in 37% yield. In analogous cases, this method of porphyrin synthesis has been used to avoid difficulties in obtaining unsymmetrical dipyrromethenes, and the decarboxylation or very low yields which may complicate the conversion of these into porphyrins (Fischer and Hofmann, *Z. physiol. Chem.*, 1937, **246**, 15). However, it rarely proceeds rationally to type-II porphyrins, and mixtures of the type isomers usually result. In the present case there was no evidence of partial decarboxylation of the side-chains. Analysis indicated an octacarboxylic ester, and paper chromatography (Nicholas and Rimington, *Biochem. J.*, 1951, **48**, 306) of the free porphyrin,



a, The synthetic ester (I*d*). *b, Carboxylated hæmatinic acid from uroporphyrin I. Both in Nujol.*

obtained from the unrecrystallized methyl ester by acid hydrolysis, gave no indication of heptacarboxylic or lower acids. When the synthesis was carried out under conditions more favourable to decarboxylation, in boiling formic acid rather than at 40°, most of the ester was extracted by boiling methanol and gave analyses for a heptacarboxylic ester. However, there is little doubt that the product obtained at 40° is a mixture of type isomers (III*a*, *b*, *c*, and *d*) in unknown proportions, rather than pure (III*b*). The melting point of the methyl ester was not altered by repeated crystallization, but prolonged extraction of the amorphous free acid with boiling acetic acid gave fractions from which methyl esters with lower melting points were obtained. Also, a low-melting mixture of coproporphyrin esters was obtained after partial decarboxylation at 190°.

The synthetic porphintetra-acetic-tetrapropionic acid, obtained by alkaline hydrolysis of its methyl ester, was oxidized to (I*d*), shown by m. p., mixed m. p., and infra-red spectra (Figure) to be identical with the analytical carboxylated hæmatinic acid, which was obtained in the same yield by oxidizing uroporphyrin I. This confirms Fischer's structure (I*d*) for the carboxylated hæmatinic acid and provides the first direct evidence that acetic acid side chains are present in uroporphyrin I.

A synthetic tetramethylporphintetra-acetic acid differed from uroporphyrin I spectroscopically and was partially decarboxylated even on alkaline hydrolysis of its ester (Fischer and Mueller, *Z. physiol. Chem.*, 1937, **246**, 31); this made it difficult to account for the

properties of uroporphyrin I in terms of (III*a*). This difficulty is removed by the similarity in properties between the synthetic porphintetra-acetic-tetrapropionic acid and uroporphyrin I. The solubilities are all of the same order, those of the synthetic porphyrin being usually somewhat greater, as would be expected in a mixture of isomers. The absorption spectra in various solvents showed no significant differences. Both free porphyrins, though stable at 100° in alkali or acetic acid, are partially decarboxylated to coproporphyrins at 190°. They were indistinguishable by paper chromatography (Nicholas and Rimington, *loc. cit.*; Nicholas and Comfort, *Biochem. J.*, 1949, **45**, 208), both giving characteristically two spots.

An unusual property common to the two porphyrins was noted when crystallization of the free synthetic porphintetra-acetic-tetrapropionic acid by Fischer and Hilger's method (*Z. physiol. Chem.*, 1925, **149**, 65) proved unsatisfactory. Irreversible changes in spectra and colour showed that both the free synthetic porphyrin and the free uroporphyrin I are unstable in hot pyridine–acetic acid, even in the dark. They are also unstable in hot N-sodium carbonate but are stable in stronger alkali such as 2N-ammonia or -sodium hydroxide. The methyl esters of both these porphyrins are stable in hot pyridine–acetic acid, as are both free coproporphyrin I and its methyl ester. This reaction is suggestive of the oxidations brought about by light, to which vinylporphyrins are particularly sensitive (cf. Fischer and MacDonald, *Annalen*, 1939, **540**, 211), and by the action of air and reducing agents on hæmin (Lemberg, *Biochem. J.*, 1935, **29**, 1322).

On this evidence, Fischer's uroporphyrin I structure can be regarded as proved only if it be assumed that all four pyrrole nuclei bear the same substituents; this assumption has been discussed from an earlier point of view by Fischer and Siebert (*Annalen*, 1930, **483**, 1) and by Fischer and Hofmann (*loc. cit.*). Though the easily decarboxylated methylmalonic acid residues may be excluded (Fischer and Zischler, *Z. physiol. Chem.*, 1937, **245**, 124), there has been no positive evidence against the presence of one pyrrole nucleus bearing methyl and succinic acid groups. More than one such is very unlikely for, though uroporphyrin I has never given more than two mols. of (I*d*) on oxidation, no isomer of it has been detected though (I*c*) is produced in very high yield on oxidation of tetramethylporphintetrasuccinic acid (Fischer and Staff, *Z. physiol. Chem.*, 1935, **234**, 97). Also (I*d*) was obtained in the same yield by oxidizing either uroporphyrin I or the synthetic porphintetra-acetic-tetrapropionic acid under identical conditions. As *meso*-substituents profoundly alter the spectra of porphyrins, the above evidence appears to exclude other alternative structures.

Proof of the absence of *C*-methyl groups would completely establish Fischer's uroporphyrin I structure (III*a*) except in the question of type. Though *C*-methyl bands appeared to be absent in the infra-red spectrum of uroporphyrin I, this evidence was treated with reserve (MacDonald, *loc. cit.*). However, it is now clear from the examination of the infra-red spectra of other porphyrins, that conclusions as to the presence or absence of *C*-methyl bands in those of the uroporphyrins must await further comparative data. Though the Kuhn–Roth *C*-methyl determinations have given apparently decisive results in favour of Fischer's structure, their validity will have to be established empirically. Further synthetic evidence could only be obtained by the synthesis of the natural uroporphyrins; these are being sought in the synthetic porphintetra-acetic-tetrapropionic acid and through further syntneses from the pyrroles (II*b* and *c*).

Experimental

M. p.s are uncorrected.

5-Carbethoxy-4-carbethoxymethyl-2-methylpyrrole-3-aldehyde (IV*b*).—A slow current of dry hydrogen chloride was passed, for 2 hours, into a solution of the pyrrole (IV*a*) (20 g.) in dry ether (60 c.c.), dry chloroform (60 c.c.), and anhydrous hydrogen cyanide (20 c.c.), the solution being protected from moisture, cooled in an ice-salt bath, and frequently shaken. Gas was passed in at an increased rate while the crystals separated and for 2 hours thereafter. The aldimine hydrochloride was filtered off, washed with ether, and dried *in vacuo*. It was dissolved in ice-water and quickly filtered, and the pH was brought to 4. The *aldehyde* (21·6 g.,

97%) soon separated; it was filtered off, washed with water, and dried *in vacuo* (m. p. 151—152°). Colourless needles, m. p. 154°, were obtained after recrystallization from ether (thimble), then from water (Found: C, 58·5; H, 6·6; N, 5·6. $C_{13}H_{17}O_5N$ requires C, 58·4; H, 6·4; N, 5·2%).

Ethyl 3-Carbethoxymethyl-4-2′-carboxyvinyl-5-methylpyrrole-2-carboxylate (IV*c*).—The aldehyde (IV*b*) (9·5 g.), 90% ethanol (40 c.c.), malonic acid (5 g.), and aniline (4 c.c.; freshly distilled) were refluxed on a steam-bath for 20 hours, then filtered hot (charcoal), and the solvent was distilled off. The crystalline residue was made into a slurry with toluene (10 c.c.), filtered off, and washed with toluene, 40% ethanol, and with light petroleum, leaving the *ester* (5·6 g., 51%), m. p. 205—207°. From 40% ethanol (charcoal), colourless prisms, m. p. 205—206° (Found: C, 59·0; H, 6·4; N, 4·9. $C_{15}H_{19}O_6N$ requires C, 58·2; H, 6·2; N, 4·5%), were obtained.

Ethyl 4-2′-Carbethoxyethyl-3-carbethoxymethyl-5-methylpyrrole-2-carboxylate (IV*d*).—The acrylic acid (IV*c*) (5·6 g.) in water (25 c.c.) and sodium hydroxide (10 c.c. of 10%) was filtered (charcoal) and shaken at 15° under hydrogen (1 atm.) with Raney nickel (2·5 c.c.). Absorption ceased after the theoretical uptake in 24 hours. The mixed esters (V*a*) and (V*a*; $CH_2{\cdot}CO_2Et$ for $CH_2{\cdot}CO_2H$) (4·6 g.), m. p. 130—160°, were precipitated with sulphur dioxide at 0°. Part (4·1 g.) of them was dissolved in hot ethanolic hydrogen chloride (25 c.c. of 5%) and poured into water after 24 hours at 20°. The *product* (4·1 g., 75%), filtered off and washed with water, had m. p. 60—63°. From light petroleum (b. p. 40—60°; thimble), colourless needles, m. p. 63—63·5° (Found: C, 60·3; H, 7·4; N, 4·2. $C_{17}H_{25}O_6N$ requires C, 60·2; H, 7·4; N, 4·1%), were obtained; Ehrlich's reaction was negative in the cold but strongly positive on heating.

The same product was obtained in lower yield by reduction of the acrylic acid in dilute sodium hydroxide with sodium amalgam at 8°, followed by esterification.

Ethyl 4-2′-Carboxyethyl-3-carboxymethyl-5-methylpyrrole-2-carboxylate (V*a*).—The acrylic acid (IV*c*) was reduced as above but for 2 days. The crude *product* was precipitated with acid, crystallized twice from water (30 parts), and sublimed ($187°/2 \times 10^{-3}$ mm.), as colourless prisms, m. p. 178° (decomp.); Ehrlich's reaction was positive in the hot (Found: C, 55·1; H, 6·05; N, 5·1. $C_{13}H_{17}O_6N$ requires C, 55·1; H, 6·0; N, 4·9%).

4-2′-Carboxyethyl-3-carboxymethyl-5-methylpyrrole-2-carboxylic Acid (V*b*).—The tri-ester (IV*d*) (1·7 g.) in ethanol (20 c.c.) and 10% aqueous sodium hydroxide (20 c.c.) was heated in an open flask on the steam-bath until dry (2·5 hours). The crystalline residue was well washed with ethanol, dissolved in water (20 c.c.), filtered (charcoal), and made acid to Congo-red with sulphur dioxide at 0°. The precipitated *acid* (1·2 g., 92%) was filtered off, washed with water, and dried *in vacuo* at 20° (m. p. 144°). After two recrystallizations from dry acetone (thimble) it formed colourless prisms, m. p. 145—146° (decomp.), Ehrlich's reaction being positive in the cold (Found: C, 52·0; H, 5·7; N, 5·2. $C_{11}H_{13}O_6N$ requires C, 51·8; H, 5·1; N, 5·5%). When dry, it slowly becomes violet, but is again obtained pure and colourless by extraction with acetone.

3-2′-Carboxyethyl-4-carboxymethyl-2-methylpyrrole (V*c*).—The tricarboxylic acid (V*b*) (460 mg.) with water (2 c.c.) was heated to effect solution at 100° (*ca.* 5 minutes) and freeze-dried. After two crystallizations from dry ether–light petroleum (b. p. 40—60°; thimble), the product was obtained as colourless needles, m. p. 126° (decomp.) (Found: C, 57·2; H, 6·4; N, 6·7. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2; N, 6·6%). Ehrlich's reaction was positive in the cold.

Decarboxylation of (V*a*) *to Carbethoxycryptopyrrolecarboxylic Acid* (VI*a*).—The mono-ester (V*a*) was heated for a few minutes at 250°, then sublimed *in vacuo* ($185°/2 \times 10^{-3}$ mm.). The product formed colourless crystals [from ether–light petroleum (b. p. 40—60°)], m. p. 154° [lit., 152°, 154°, and 159° (Fischer and Andersag, *loc. cit.*; Siedel and Winkler, *Annalen*, 1943, **554**, 167, 193) (Found: C, 60·4; H, 7·3; N, 6·2. Calc. for $C_{12}H_{17}O_4N$: C, 60·2; H, 7·2; N, 5·9%).

Degradation of (IV*d*) *to Carbethoxycryptopyrrolecarboxylic Acid* (VI*a*).—The tri-ester (IV*d*) (545 mg.) was heated under reflux for 4 hours in ethanol containing sodium hydroxide (150 mg.). The solvent was distilled off, the residue dissolved in water, and the solution acidified. The impure mono-ester (V*a*) was extracted from the precipitate with ether (thimble) and decarboxylated to (VI*a*), which melted at 154° after successive crystallizations from ether, dilute ethanol, and water. Ehrlich's reaction was negative in the cold, positive in the hot.

Degradation of the Tricarboxylic Acid (V*b*) *to Cryptopyrrolecarboxylic Acid* (VI*c*).—The tricarboxylic acid (V*b*) (220 mg.) was heated with glycerol (bath, 210°) until no more gas was evolved; water was added and the product (VI*c*) extracted with ether. It formed pale tan crystals (from water), m. p. 136°, mixed m. p. 136—137° with authentic material of m. p. 138°; Ehrlich's reaction was positive in the cold.

Ethyl 2-Bromomethyl-3-2′-carbethoxyethyl-4-carbethoxymethylpyrrole-5-carboxylate (IV*e*) *and Diethyl 5 : 5-Dicarbethoxy-3 : 3′-bis-2″-carbethoxyethyl-4 : 4′-biscarbethoxymethyldipyrrylmethane* (VII*a*).—(*a*) The tri-ester (IV*d*) (1 g.) in acetic acid (0·3 c.c.) was treated with bromine in acetic acid (1 c.c. containing 0·5 g. of bromine) at 30°. After some hours, the solvent was removed *in vacuo*, leaving the α-bromomethyl derivative (IV*e*) as an oil. This was boiled for 3 hours with water (500 c.c.), and the tar obtained on cooling was crystallized from 50% aqueous ethanol (8 c.c.), to give the *dipyrrylmethane* (VII*a*) (0·17 g., 17%), m. p. 95—97° (halogen absent; Beilstein test). For analysis it was recrystallized twice from hexane (thimble), forming large pale tan-coloured plates, m. p. 100·5° (Found: C, 60·1; H, 7·2; N, 4·4. $C_{33}H_{46}O_{12}N_2$ requires C, 59·8; H, 7·0; N, 4·2%).

(*b*) The tri-ester (IV*d*) (1·25 g.) in carbon disulphide (1 c.c.) was treated with bromine in carbon disulphide (0·6 g. in 2·5 c.c.) at 20°. After a few minutes, the solvent was removed *in vacuo*, and the oily bromomethyl derivative (IV*e*) washed twice with water by decantation, and dried *in vacuo*. It was heated under reflux with ethanol (5 c.c.) for 4 hours, most of the solvent was distilled off, and the residue seeded and left at 0°. The product (VII*a*) (0·45 g., 37%) remained after draining on a porous tile. It was pure enough for the next step.

Better yields of a mixed ester (60—80%) have since been obtained by brominating the dimethyl ester of (V*a*) and boiling the product with methanol.

5 : 5′-Dicarboxy-3 : 3′-bis-2″-carboxyethyl-4 : 4′-biscarboxymethyldipyrrylmethane (VII*b*).—The dipyrrylmethane (VII*a*) (0·8 g.) in ethanol (4·5 c.c.) and aqueous sodium hydroxide (4·5 c.c. of 10%) was refluxed for 2 hours, the ethanol distilled off, and the residue cooled and diluted to 10 c.c. After filtration (charcoal) and acidification with sulphur dioxide at 0°, the *product* (0·51 g., 86%) soon separated and was dried *in vacuo* [m. p. 146° (decomp.)]. Recrystallized from dry acetone (thimble), it formed somewhat hygroscopic, colourless crystals, m. p. 157° (decomp.) (Found: C, 50·8; H, 4·8; N, 5·55. $C_{21}H_{22}O_{12}N_2$ requires C, 51·0; H, 4·5; N, 5·7%).

2 : 3 : 6 : 7-Tetrabis-2″-carbomethoxyethyl-1 : 4 : 5 : 8-tetrabiscarbomethoxymethylporphin and Type Isomers (III*b*, *a*, *c*, *and d*) *(Octamethyl Porphintetra-acetate-tetrapropionate)*.—A stream of air was passed through a suspension of the dipyrrylmethane (VII*b*) (2·08 g.) in 98% formic acid (50 c.c.) at 40° for 5 days, the volume being maintained by adding acid. The porphyrin was then precipitated by pouring the mixture into saturated brine (500 c.c.) and adjusting the pH to about 3 with sodium hydroxide. It was filtered off and washed successively with brine, water, and methanol; a little acetic acid had been added to each of these to prevent peptization. The product was dissolved in methanolic hydrogen chloride (100 c.c.; saturated at 0°), and the solution left for 1 day, diluted with chloroform (200 c.c.), and poured into ice-water. The chloroform layer was washed with water, very dilute sodium hydroxide, and again water. After being dried (Na_2SO_4), the solution was filtered through a column of neutral alumina and the pigment washed through with more chloroform. The filtrate and washings were filtered and concentrated. On addition of hot methanol the *product* (732 mg., 37%) separated as hair-like needles, m. p. 256—258° (block), m. p. unchanged after four recrystallizations from chloroform–methanol (66% recovery) (Found: C, 61·15; H, 5·8; N, 6·1; OMe, 27·9; *C*-Me 0·0. $C_{48}H_{54}O_{16}N_4$ requires C, 61·1; H, 5·8; N, 5·9; OMe, 26·3%).

The ester is soluble in hot ethyl acetate, but insoluble in ether and methanol. When solutions in acid are neutralized, ether extracts about five times as much of this ester as it does of uroporphyrin I ester. In 25% hydrochloric acid, the spectra of the synthetic ester and of uroporphyrin I methyl ester could not be distinguished with a comparison spectroscope. The spectra were measured in chloroform (dried with sulphuric acid and then potassium hydroxide, stabilized with 5% v/v of dry ether) (Unicam) (figures in parentheses are $10^{-4}\varepsilon$): Synthetic ester (80 mg./l.), max. at 626 (0·377), 572 (0·669), 536 (0·897), 502 (1·356), 406 (20·65), inflexion at 595—597 (0·139), min. at 609 (0·084), 554 (0·148), 522 (0·330), 459 mμ (0·186). Uroporphyrin ester (70 mg./l.), max. at 626 (0·383), 572 (0·680), 537 (0·912), 502 (1·568), 406 (20·03), inflexion at 596—598 (0·146), min. at 607 (0·077), 554 (0·167), 522 (0·352), 458 (0·193). Here, as elsewhere unless otherwise indicated, uroporphyrin I methyl ester refers to products, m. p. *ca.* 283°, obtained from the urine of a case of congenital porphyria by the method of Fischer and Orth (*op. cit.*, p. 514, method a).

Porphintetra-acetic-tetrapropionic Acid (Mixed Isomers).—The synthetic ester (80 mg.) was refluxed with N-sodium hydroxide (10 c.c.) for 5 hours, then diluted with water, and acetic acid was added. The dried precipitate was dissolved in pyridine and the *acid* (53 mg.) precipitated by addition of hot acetic acid to the filtered solution; the microscopic stout needles, still contaminated with amorphous material after a second crystallization, were dried at 80°/5 × 10^{-4}

mm. (Found: C, 56·3; H, 4·6; N, 6·9. $C_{40}H_{38}O_{16}N_4$ requires C, 57·8; H, 4·6; N, 6·75%). The acid hydrolysis of the ester gave a product which was no better.

On extraction of its solutions in alkali with ether and acetic acid, traces of the porphyrin can be detected in the ether spectroscopically. When alkaline solutions were acidified with mineral acid to pH 3, ethyl acetate extracted about 15 times as much of this porphyrin as it did of uroporphyrin I (measured by ultra-violet fluorescence). The amorphous synthetic porphyrin is very slightly soluble in boiling acetic acid, being incompletely dissolved after 6 hours' extraction (thimble).

The synthetic ester was heated under reflux with 10% aqueous sodium hydroxide for 10 hours, and the free porphyrin precipitated and extracted with boiling acetic acid for 6 hours (thimble). The porphyrin in solution was precipitated, esterified with methanolic hydrogen chloride, and crystallized from chloroform–methanol (Found: C, 61·3; H, 5·9%).

In 10% aqueous sodium hydroxide, the spectra of the synthetic porphyrin and of uroporphyrin I were identical (comparison spectroscope), as were those of their copper complexes.

The Carboxylated Hæmatinic Acid (Id).—The synthetic octamethyl porphintetra-acetate-tetrapropionate (150 mg.) was hydrolysed by 5 hours' refluxing with N-sodium hydroxide (5 c.c.). After evaporation, the residue was dissolved in 50% (v/v) sulphuric acid (9 c.c.), and chromic acid (220 mg. in 1 c.c. of water) was dropped in at 0° during 1 hour. After being kept overnight at 0°, the filtered solution was diluted with water (4 c.c.) and repeatedly extracted with pure ether. The ether was removed from the extract, and the residue dissolved in 0·75N-sodium carbonate (4 c.c.) and extracted with ether. The carbonate solution was brought to pH 1 with sulphuric acid, saturated with ammonium sulphate, and repeatedly extracted with ether. This extract was dried (Na_2SO_4) and the ether evaporated off, leaving the crystalline product; recrystallized from dry ether (5 c.c.; thimble) and dried (60°/3 × 10^{-4} mm.), this formed colourless prisms (25 mg.), m. p. 179° (decomp.) (Found: C, 47·7; H, 4·25; N, 6·2. Calc. for $C_9H_9O_6N$: C, 47·6; H, 4·0; N, 6·2%). Infra-red spectrum in Nujol: Fig. (*a*).

The analytical carboxylated hæmatinic acid (24 mg.), obtained by oxidizing uroporphyrin I methyl ester (151 mg.) in the same way, had m. p. 178° (decomp.) alone or mixed with the synthetic product. In all cases sintering began at about 165° but was never considerable, The m. p.s depend on the rate of heating (here 1°/min.), and so were determined in pairs (lit., 188°, 179—180°, 178°, 184° or 176°, 168° for the analytical product; Fischer, *Z. physiol. Chem.*, 1916, **98**, 78; Fischer and Holt, *loc. cit.*; Fischer and Staff, *Z. physiol. Chem.*, 1934, **234**, 97; Fischer and Hofmann, *loc. cit.*; Fischer, Hartmann, and Riedl, *Annalen*, 1932, **494**, 246). Infra-red spectrum in Nujol: Fig. (*b*).

Partial Decarboxylation of the Synthetic Porphintetra-acetic-tetrapropionic Acid to Coproporphyrins (cf. Fischer and Zerweck, *loc. cit.*).—The porphyrin ester (44 mg.) was hydrolysed in concentrated hydrochloric acid overnight at 20°, the acid diluted to 1%, and the mixture heated for 4 hours at 185—195°. The resulting porphyrin was fractionated between hydrochloric acid and ether, esterified with diazomethane, and again fractionated. The porphyrin left on evaporation of the ether was dissolved in chloroform and filtered through a column of alumina, then crystallized by addition of hot methanol to the concentrated solution giving a mixture (13 mg.) of prismatic needles, m. p. *ca.* 180°, and radiating clusters of needles, m. p. *ca.* 135°. Recrystallization from chloroform–methanol (thimble) gave irregular aggregates of prismatic needles (6 mg.), m. p. 183° (block) (Found: C, 67·6; H, 6·8. Calc. for $C_{40}H_{46}O_8N_4$: C, 67·6; H, 6·5%). The mother-liquors deposited radiating clusters of needles (2 mg.), m. p. 134—135° (block); this m. p. has been recorded for coproporphyrin III ester but the infra-red spectra preclude identity.

No products other than coproporphyrins were detected; the crude free porphyrin was not extracted by ether from 0·2% hydrochloric acid, and the ester was extracted from ether by 2% hydrochloric acid. The esters were spectroscopically identical with coproporphyrin I in chloroform (comparison spectroscope).

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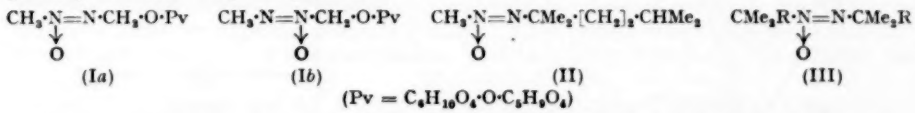
807. *Macrozamin. Part III.* Azoxymethane and Some Simple Analogues.*

By B. W. Langley, B. Lythgoe, and L. S. Rayner.

The formerly unknown primary aliphatic azoxy-compounds can be obtained by oxidising the corresponding azo-compounds with perbenzoic acid. Spectroscopic and chemical properties of azoxymethane and some of its symmetrically substituted analogues are described and compared with those of macrozamin.

Evidence outlined in Part II * led us to formulate macrozamin, the toxic β-primeveroside of *Macrozamia* species, as a substituted azoxymethane of the structure (I*a* or *b*). Primary azoxy-compounds were hitherto unknown; their synthesis and examination have now been effected as a step towards synthesis of the natural compound, and also as a means of confirming our structural conclusions and of deciding between the two structures.

With one exception the classical methods for synthesising aromatic azoxy-compounds are not well fitted for use with aliphatic compounds unless purely tertiary representatives are required, although recently, by condensing *N*-methylhydroxylamine and 2 : 5-dimethyl-2-nitrosohexane, Aston and Jenkins obtained material which was considered to be the mixed primary-tertiary compound (II) (*Nature*, 1951, **167**, 863). The only method which promised to be at all general was that involving oxidation of azo-compounds. Its first use in the aliphatic series was recorded by Aston and Parker (*J. Amer. Chem. Soc.*, 1934, **56**, 1387) who prepared the tertiary compound (III; R = CO_2Et) by use of hydrogen peroxide in acetic acid as the oxidant; this was extended by us (Part II, *loc. cit.*) to the preparation of the secondary representative azoxy*cyclo*hexane, using nitric acid as the oxidant. Attempts have now been made to extend the scope of the method to simpler primary and secondary compounds.

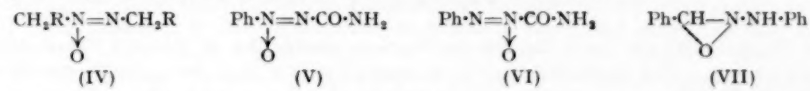


(I*a*) (I*b*) (II) (III)

(Pv = $C_6H_{10}O_4$·O·$C_5H_9O_4$)

Neither hydrogen peroxide in acetic acid nor nitric acid oxidised 2-azopropane or 1-azo-*n*-heptane to the azoxy-compounds; apparently acid-catalysed isomerisation to hydrazones took place before oxidation. This was overcome by using the relatively weakly acidic aromatic per-acids as oxidising agents; the best and most rapid-acting was perbenzoic acid, which converted azo*cyclo*hexane quantitatively into azoxy*cyclo*hexane.

This reagent yielded azoxymethane (IV; R = H) from azomethane, 1-azoxypropane (IV; R = Et) from 1-azopropane, 2-azoxypropane (III; R = H) from 2-azopropane, and ω-azoxy-*p*-chlorotoluene (IV; R = CH_2·C_6H_4Cl-*p*) from ω-azo-*p*-chlorotoluene. [1-Azopropane and ω-azo-*p*-chlorotoluene were prepared by reducing the corresponding azines to hydrazo-compounds, in the former case catalytically, in the latter with sodium amalgam and alcohol, and oxidising the hydrazo-compounds with mercuric oxide in ether.] Alone among the azo-compounds tested, ethyl azoformate was not oxidised by perbenzoic acid, but this was not unexpected since the inhibiting effect of an adjacent carbonyl group was apparent from Angeli's finding that phenylazoformamide and hydrogen peroxide in acetic acid give only (V) and no (VI) (*Atti R. Accad. Lincei*, 1917, **26**, i, 210).



(IV) (V) (VI) (VII)

The compound which Kijner (*J. Russ. Phys. Chem. Soc.*, 1899, **31**, 872) obtained by treating *N*-bromomenthylamine with silver oxide, and described as menthone menthyl-

* Part II, *J.*, 1951, 2309.

hydrazone, was oxidised by perbenzoic acid to 3-azoxy-*p*-menthane; so at first it was thought that oxidation of hydrazones might provide a valuable alternative route to azoxy-compounds. Consequently the compound which Bergmann, Ulpts, and Witte (*Ber.*, 1923, **56**, 679) obtained by the action of perbenzoic acid on benzaldehyde phenylhydrazone, and to which they assigned the structure (VII), was re-examined. Its properties convinced us that, whatever its structure, it was not the expected azoxy-compound, and this in turn threw doubt on the nature of Kijner's "menthone menthylhydrazone." The latter's ultra-violet spectrum resembled closely those of authentic azo-compounds (Fig. 1), and its infra-red absorption spectrum showed no bands in the 6μ region corresponding to a C=N group. It must therefore be reformulated as 3-azo-*p*-menthane, a structure consistent with its formation and oxidation and hydrolysis products.

Of the new azoxy-compounds ω-azoxy-*p*-chlorotoluene was solid, the others were colourless liquids of relatively high boiling points for their molecular size; azoxymethane

FIG. 1. *Ultra-violet light absorption of Kijner's compound (A), azocyclohexane (B), and 2-azopropane (C) in alcohol.*

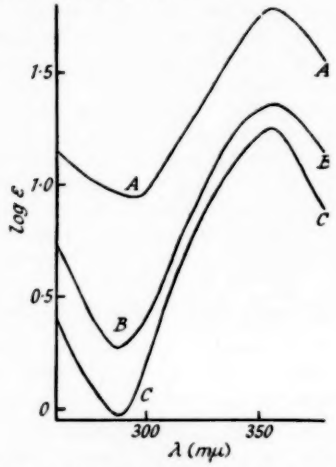
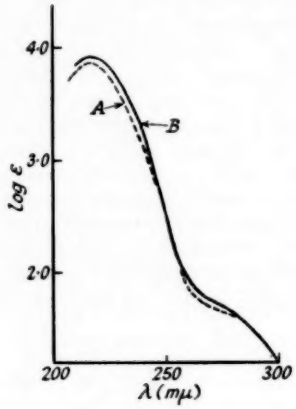


FIG. 2. *Light absorption of azoxymethane (A) and macrozamin (B) in alcohol.*



had b. p. 98° (cf. azomethane, b. p. 1·5°), and was completely miscible with water, but the azopropanes were immiscible. The ultra-violet spectra of the new primary compounds resembled those of the secondary and tertiary compounds qualitatively, showing a maximum at short wave-lenths and an inflection. As shown in Table 1 the positions of these features

TABLE 1. *Light absorption of azoxy-compounds in alcohol.*

	Maximum		Inflection	
Compound	λ(mμ)	log ε	λ(mμ)	log ε
2-Azoxy-2 : 5-dimethylhexane [a]	223	3·75	287	1·58
2-Azoxypropane	220·5	3·84	278	1·72
1-Azoxypropane	217	3·86	277	1·75
Azoxymethane	217	3·86	274	1·64
Macrozamin [a]	217	3·92	273	1·72

[a] Part II, *loc. cit.*

depend characteristically upon the size and tertiary, secondary, or primary nature of the attached groups. The extinction curves of azoxymethane and macrozamin correspond very closely (Fig. 2).

In Part II, the strong bands at 1531 and 1546 cm.$^{-1}$ in the infra-red spectra of macrozamin and its hexa-acetate were provisionally identified as due to the asymmetric stretching of the azoxy-group; the correlation was not completely certain because for the synthetic

compounds then available the corresponding frequency was much lower (*ca.* 1500 cm.$^{-1}$). The data obtained from the new compounds remove this uncertainty and enable the identification of a further band, due to symmetric stretching of the azoxy-group, in the spectra of macrozamin and its hexa-acetate. The spectrum of azoxymethane is very simple in the 4—8-μ region, consisting of four very strong absorption bands at 1342, 1382, 1439, and 1527 cm.$^{-1}$; the bands at 1382 and 1439 cm.$^{-1}$ clearly correspond to C–H deformation modes. Those at 1342 and 1527 cm.$^{-1}$ are assigned respectively to symmetric and asymmetric stretching modes of the azoxy-group; the corresponding vibrations of the electronically similar nitro-group in nitromethane cause bands at 1379 and 1570 cm.$^{-1}$ (Smith, Pan, and Nielsen, *J. Chem. Phys.*, 1950, **18**, 706). The relevant frequencies for other azoxy-compounds vary in a characteristic way with the size and primary, secondary, or tertiary nature of the attached groups (see Table 2), so that although the values for the

TABLE 2. *Characteristic frequencies of the azoxy-group.*

Compound	State	Symmetric stretching (cm.$^{-1}$)	Asymmetric stretching (cm.$^{-1}$)
2-Azoxy-2 : 5-dimethylhexane	Liquid	1285 s	1495 vs
Azoxy*cyclo*hexane	,,	1285 s	1495 vs
2-Azoxypropane	,,	1295 vs	1500 vs
1-Azoxypropane	,,	1316 s	1506 vs
Azoxymethane	,,	1342 vs	1527 vs
Hexa-acetyl macrozamin	Nujol mull	1344 s	1531 s

tertiary compounds investigated in Part II differ by up to 60 cm.$^{-1}$ from those of hexa-acetyl macrozamin, those of azoxymethane and hexa-acetyl macrozamin are almost identical. These results reinforce those from the ultra-violet spectra and leave little doubt, not merely that macrozamin contains an azoxy-group, but that it is a substituted azoxymethane.

Chemical examination of the primary and secondary azoxy-compounds was limited to the effect of acids, alkalis, and reducing agents; these are characteristic reagents for macrozamin and also for aliphatic nitro-compounds. Since azoxy-compounds are, formally, the nitrogen analogues of nitro-compounds, some similarity between the two classes was expected.

Azoxy*cyclo*hexane was not reduced by lithium aluminium hydride in boiling ether, although this reagent reduced azoxybenzene to azobenzene, and 2-nitrobutane to 2-aminobutane (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3739). ω-Azoxy-*p*-chlorotoluene was reduced to ω-azo-*p*-chlorotoluene by magnesium and methanol, but some further reduction to the hydrazo-compound also took place. Azoxymethane and 1-azoxypropane were reduced smoothly to the corresponding hydrazo-compounds by stannous chloride in hydrochloric acid. Like that of macrozamin, catalytic reduction of the primary and secondary azoxy-compounds at room temperature required the presence of a mineral acid, but the course of the reduction of the synthetic compounds was different in that, with one exception, only 2 mols. of hydrogen were absorbed, the link between the two nitrogen atoms being preserved intact and a *NN'*-dialkylhydrazine formed. The exceptional compound was ω-azoxy-*p*-chlorotoluene, which absorbed 11 mols. of hydrogen, giving hexahydrobenzylamine. It is thus clear that constitutional factors may determine a reductive fission of the linked nitrogen atoms, and the fission which occurs with macrozamin is clearly due to the presence of the primeverosyloxy-substituent, but the way in which its effect is exercised remains obscure.

It had been expected that the primary azoxy-compounds might contain readily ionisable C–H links adjacent to the quatercovalent nitrogen atom, but azoxymethane did not behave as a pseudo-acid when titrated with alkali, and ω-azoxy-*p*-chlorotoluene, where the effects of phenyl and azoxy-groups should reinforce each other in promoting ionisation, was insoluble in dilute aqueous alkali. Azoxymethane and 1-azoxypropane were decomposed by hot concentrated aqueous alkali with the formation of volatile bases. It was of interest that from azoxymethane, but not from 1-azoxypropane, some cyanide ion was formed under these conditions; nitromethane also gives cyanide ion on treatment with

alkali, presumably by decomposition of methazonic acid (Dunstan and Dymond, *J.*, **1891**, **59**, 430). The similar behaviour of azoxymethane may be related to the formation of cyanide ion from macrozamin (Part II, *loc. cit.*), for which, however, very much milder alkaline conditions suffice.

Possibly the most interesting reactions of the primary and secondary azoxy-compounds were those with hot aqueous hydrochloric acid. The secondary compounds reacted principally thus :

$$R_2CH{\cdot}\underset{\downarrow}{\underset{O}{N}}{=}N{\cdot}CHR_2 + H_2O \longrightarrow 2R_2CO + NH_2{\cdot}NH_2$$

Azoxy*cyclo*hexane gave hydrazine (0·6 mol.) together with *cyclo*hexanone and dodecahydrotriphenylene; it was shown that, although the latter is not formed from interaction of hydrochloric acid and *cyclo*hexanone alone, it is produced in comparatively high yield when hydrazine is present. 2-Azoxypropane also gave hydrazine (0·6 mol.) but the acetone formed simultaneously was destroyed.

Closely related to these decompositions is that which α-azoxy*iso*butyric acid (III; R = CO_2H) undergoes in hot water; it was noticed but not further investigated by Aston and Parker (*loc. cit.*). Quantitative determinations showed that it proceeds in approximate accordance with the expression :

$$2(HO_2C{\cdot}CMe_2{\cdot})_2(N_2O) + H_2O \longrightarrow CHMe_2{\cdot}CO_2H + 3Me_2CO + 3CO_2 + N_2H_4 + N_2.$$

In view of the ready decarboxylation of α-nitro- and α-azo-acids, the nature and proportions of the products of the above reaction suggest two simultaneous reactions of about equal speed involving initial loss of, respectively, one and two molecules of carbon dioxide. It is however unlikely that the expected azoxy-compounds were actually formed as intermediates, since 2-azoxypropane would certainly have survived the prevailing conditions.

The primary azoxy-compounds were converted by hot hydrochloric acid into carboxylic acids and monosubstituted hydrazines; thus azoxymethane gave formic acid and methylhydrazine (0·9 mol.), and 1-azoxypropane gave propionic acid and *n*-propylhydrazine (0·9 mol.). Prolonged treatment of ω-azoxy-*p*-chlorotoluene gave *p*-chlorobenzoic acid and *p*-chlorobenzylhydrazine, but briefer treatment gave largely *N*-*p*-chlorobenzoyl-*N'*-*p*-chlorobenzylhydrazine, the structure of which was shown by hydrolysis. Clearly the reaction takes place in two steps, the first an acid-catalysed isomerisation to a *N*-acyl-*N'*-alkylhydrazine, which is then hydrolysed, rapidly if the acyl group is of the Alk·CO type, but more slowly if it is of the Ar·CO type. The reaction is closely similar to that undergone by primary aliphatic nitro-compounds in 85% sulphuric acid (Lippincott and Mass, *Ind. Eng. Chem.*, 1939, **31**, 118) :

$$R{\cdot}CH_2{\cdot}\underset{\downarrow}{\underset{O}{N}}{=}N{\cdot}CH_2{\cdot}R \xrightarrow{H^+} R{\cdot}CO{\cdot}NH{\cdot}NH{\cdot}CH_2{\cdot}R \xrightarrow[H_2O]{H^+} R{\cdot}CO_2H + NH_2{\cdot}NH{\cdot}CH_2{\cdot}R$$

$$R{\cdot}CH_2{\cdot}N\begin{matrix}=O\\ \searrow O\end{matrix} \xrightarrow{H^+} R{\cdot}CO{\cdot}NH{\cdot}OH \xrightarrow[H_2O]{H^+} R{\cdot}CO_2H + NH_2{\cdot}OH$$

both reactions have as driving force the tendency of highly oxidised nitrogen systems to achieve a lower oxidation level by oxidising adjacent methylene or methine groups.

Azoxymethane was converted into formic acid and methylhydrazine at room temperature by ethereal hydrogen chloride, and formylhydrazine was similarly hydrolysed to hydrazine, the small amounts of water necessary for these changes gaining entry through the calcium chloride guard-tube of an apparatus with ground joints. Consequently, a logical interpretation can be given of the behaviour of macrozamin towards hydrochloric acid under two different sets of conditions. The reaction with hot aqueous acid, which gives the component sugars, methanol, formaldehyde, and nitrogen, is initiated by hydrolysis of the molecule at the glycosidic link. When the hexa-acetate is treated with ethereal hydrogen chloride, the products identified are hydrazine and formaldehyde (Part II); clearly water is then present in such low concentration that the hydrolysis at the glycosidic

link is suppressed and, instead, oxidation–reduction of the azoxymethane part of the molecule takes place, giving a sensitive intermediate which is gradually hydrolysed as the necessary water is absorbed :

$$CH_3\cdot\overset{\downarrow}{N}(O)=N\cdot CH_2\cdot O\cdot Pv' \xrightarrow{H^+} OHC\cdot NH\cdot NH\cdot CH_2\cdot O\cdot Pv' \xrightarrow[H_2O]{H^+,-} H\cdot CO_2H + N_2H_4 + CH_2O + Pv'OH$$

$$[Pv' = \cdot C_6H_7O(OAc)_3\cdot O\cdot C_5H_6O(OAc)_3]$$

The production of hydrazine rather than methylhydrazine, and of formaldehyde, shows that it is the methyl, not the methylene group of the aglycone which has been oxidised. From this, it would clearly be possible to decide between the two structures (I*a* and *b*) for macrozamin, provided the exact course of the acid-catalysed isomerisation of primary azoxy-compounds were known.

We regard it as very probable that the correct structure is (I*a*), since we believe such isomerisations are structurally specific, and that oxidation occurs at the methylene group adjacent to the quatercovalent and more highly oxidised nitrogen atom of the azoxy-group, and not at that adjacent to the tervalent nitrogen atom. However, a direct verification of this view is perhaps desirable, because acid hydrolysis of secondary azoxy-compounds is accompanied by the equal oxidation of both the adjacent methine groups. For this verification the preparation, structural determination, and hydrolysis of isomeric pairs of unsymmetrically substituted primary azoxy-compounds are clearly necessary, and appropriate experiments are in progress.

Experimental

Azoxymethane.—A conventional vacuum trap, the inlet tube of which was equipped with a tap, was connected through a delivery tube of bore not less than 8 mm. to a flask (1 l.) provided with a wide-bore spiral condenser protected by an efficient calcium chloride tube. The flask contained perbenzoic acid (30 g.) in dry ether (20 c.c.), and initially the delivery tube from the trap was raised above the surface of the solution. The trap and condenser were cooled in acetone–carbon dioxide, and the flask in ice, and azomethane (10 g.; Thiele, *Ber*, 1909, **42**, 2578), dried by passage over calcium chloride, was distilled through the inlet tube into the trap. The delivery tube was then lowered just below the surface of the liquid in the flask, and the inlet tube was connected to a source of dry nitrogen, which was admitted through the tap at such a rate that *ca.* 2 bubbles per second emerged from the delivery tube. The trap was allowed to warm slowly, so that the azomethane was transferred during ½ hour to the flask. The nitrogen current was continued for a further ½ hour, the condenser rinsed into the flask with a little dry ether, and the flask then removed from its cooling-bath, disconnected from the rest of the apparatus, and connected at once to a vacuum line through a series of traps cooled in liquid nitrogen. The volatile contents of the reaction flask were transferred to the traps during 24 hours at 1 mm. pressure, and the ethereal distillate so obtained, after drying ($CaSO_4$), was fractionally distilled with the aid of a short but efficient column (Dixon, *J. Soc. Chem. Ind.*, 1949, **68**, 299), giving *azoxymethane* (7 g.), b. p. 98°/760 mm., n_D^{17} 1·4300 [Found : C, 32·7; H, 8·3%; *M* (Regnault bulb), 71. $C_2H_6ON_2$ requires C, 32·4; H, 8·1%; *M*, 74]. The combustion was carried out in a current of air as the use of oxygen with azoxymethane and the azoxypropanes led to explosions. Nitrogen determinations by the Dumas method gave low and inconsistent values for azoxymethane.

NN′-*Di*-n-*propylhydrazine.*—Freshly distilled propaldazine in alcohol (5 vols.) was hydrogenated in contact with Adams's platinic oxide at room temperature and 5 atm.; 12 hours were required for the uptake of 2 mols. of hydrogen. Concentrated hydrochloric acid was then added, the catalyst filtered off, and the solution evaporated under reduced pressure. Repeated recrystallisation of the residue from alcohol gave the base *dihydrochloride* (30%) which evolved hydrogen chloride when heated and had m. p. *ca.* 160° (decomp.) (Found : C, 38·2; H, 9·4; N, 14·8. $C_6H_{16}N_2Cl_2$ requires C, 38·1; H, 9·5; N, 14·8%). The *bis*-3 : 5-*dinitrobenzoyl* derivative formed crystals (from acetic acid), m. p. 200° (Found : C, 47·5; H, 4·0; N, 16·8. $C_{20}H_{20}O_{10}N_6$ requires C, 47·6; H, 4·0; N, 16·7%).

1-*Azopropane.*—The above dihydrochloride (10 g.) was added to a solution of sodium hydroxide (10 g.) in water (20 c.c.), and the mixture extracted with ether (4 × 10 c.c.). The

ethereal extract was washed with a little water and then shaken with mercuric oxide (13 g.) for 1 hour, dried (Na_2SO_4), and filtered. Fractional distillation of the filtrate in nitrogen gave 1-*azopropane* (3·8 g.) as a pale yellow liquid, b. p. 104°, n_D^{20} 1·4060 (Found : N, 24·4. $C_6H_{14}N_2$ requires N, 24·6%).

1-*Azoxypropane*.—A solution of 1-azopropane (10 g.) in dry methylene dichloride (20 c.c.) was cooled to 0° and perbenzoic acid (14 g.) in methylene dichloride (40 c.c.) added during 1 hour; the reaction was vigorous and benzoic acid separated from solution. After it had been kept for a further ½ hour the solution was treated with excess of 10% aqueous potassium iodide, followed at once by an excess of aqueous sodium thiosulphate. The methylene dichloride layer was separated, washed with N-sodium hydroxide, then with water, dried, and fractionally distilled under reduced pressure (Dixon column; *loc. cit.*). 1-*Azoxypropane* (7·9 g.) was obtained with b. p. 67°/20 mm., d^{20} 0·902, n_D^{20} 1·4365 (Found : C, 55·2; H, 10·5; N, 21·4. $C_6H_{14}ON_2$ requires C, 55·4; H, 10·8; N, 21·5%).

2-*Azoxypropane*.—2-Azopropane (5·4 g.; Lochte, Bailey, and Noyes, *J. Amer. Chem. Soc.*, 1922, **44**, 2556) was oxidised in methylene dichloride as described for 1-azopropane. Fractional distillation gave 2-*azoxypropane* (3·6 g.), b. p. 38°/14 mm. (Found : C, 54·9; H, 10·6; N, 21·5%).

NN′-*Di*-p-*chlorobenzylhydrazine*.—To *p*-chlorobenzaldazine (22·8 g.) in boiling alcohol (690 c.c.) 4% sodium amalgam (690 g.) was added during 3 hours and the mixture heated under reflux for a further 4 hours and then filtered. The filtrate was concentrated under reduced pressure in nitrogen to *ca.* 150 c.c., poured into cold water (1·5 l.), and extracted with ether (3 × 250 c.c.). The ethereal extract was shaken with 2N-hydrochloric acid (110 c.c.) at 0°, giving a thick white precipitate which was collected and recrystallised from alcohol. The base *hydrochloride* (16 g.) was obtained as needles, m. p. 215—216° (decomp.) (Found : C, 53·2; H, 5·5; N, 9·2; Cl′, 11·2. $C_{14}H_{15}N_2Cl_3$ requires C, 53·0; H, 4·7; N, 8·8; Cl′, 11·2%).

ω-*Azo*-p-*chlorotoluene*.—The above hydrochloride (4 g.), 10% aqueous sodium hydroxide (40 c.c.), and ether (50 c.c.) were shaken together until all the solid had dissolved. The ethereal layer was removed, the alkaline layer extracted with more ether, and the combined ethereal layers were washed with a little water, dried briefly, and then shaken for 6 hours with mercuric oxide (4 g.). The mixture was filtered, the filtrate evaporated to dryness, and the residue crystallised from a little alcohol, giving ω-*azo*-p-*chlorotoluene* (2·7 g.), m. p. 89—90° (Found : C, 60·7; H, 4·5; N, 10·4. $C_{14}H_{12}N_2Cl_2$ requires C, 60·2; H, 4·3; N, 10·0%).

ω-*Azoxy*-p-*chlorotoluene*.—The azo-compound (2·46 g.) in chloroform (10 c.c.) was added slowly to a stirred and cooled solution of perbenzoic acid (1·33 g.) in chloroform (23 c.c.), the solution kept at 0° overnight, and then freed from perbenzoic and benzoic acids in the usual manner and evaporated. Crystallisation of the residue from alcohol gave ω-*azoxy*-p-*chlorotoluene* (2·5 g.) as needles, m. p. 103° (Found : C, 57·1; H, 4·2; N, 9·8. $C_{14}H_{12}ON_2Cl_2$ requires C, 57·0; H, 4·1; N, 9·5%). Light absorption in alcohol : max. at 218 mμ, ε 27,700.

Reduction of ω-*Azoxy*-p-*chlorotoluene with Magnesium and Methanol*.—The azoxy-compound (0·3 g.), magnesium turnings (0·5 g.), and dry methanol (20 c.c.) were heated together under reflux till all the magnesium had dissolved (2 hours). The cooled mixture was diluted with water and extracted with ether. Evaporation of the ethereal extract gave an oil which was dissolved in methanol, whereupon it slowly deposited ω-azo-*p*-chlorotoluene, m. p. 89—90°, undepressed on admixture with authentic material. A portion of the mother-liquor reduced mercuric oxide, showing the presence of a hydrazine derivative, so the rest was treated with hydrogen chloride, *NN′*-di-*p*-chlorobenzylhydrazine being obtained as the hydrochloride, m. p. 211—212° (decomp.).

Reduction of Azoxymethane with Stannous Chloride.—A solution of stannous chloride dihydrate (1 g.) in cold 12N-hydrochloric acid (2 c.c.), and azoxymethane (280 mg.), were kept together overnight, then diluted with water (30 c.c.), and freed from tin by hydrogen sulphide. Evaporation of the filtered solution gave crystalline *NN′*-dimethylhydrazine dihydrochloride, which was identified by conversion into the dibenzoyl derivative, m. p. 87°, undepressed on admixture with authentic material.

Catalytic Reduction of Azoxy-compounds.—(*a*) 1-Azoxypropane (1·18 g.) in methanol (10 c.c.) was added to pre-reduced Adams's platinic oxide (48 mg.) in methanol (30 c.c.), and the mixture shaken at room temperature and pressure with hydrogen, but none was absorbed. Addition of hydrochloric acid (1 c.c.; *d* 1·16) caused rapid absorption of 2 mols. of hydrogen; the filtered solution gave on evaporation a crystalline solid (1·61 g.) identified as *NN′*-di-1-propylhydrazine dihydrochloride by conversion into the bis-3 : 5-dinitrobenzoyl derivative, m. p. 200°.

(*b*) The following reductions, each involving absorption of 2 mols. of hydrogen, were carried out as described above. Azoxymethane gave *NN'*-dimethylhydrazine, identified as the dibenzoyl derivative, m. p. 87°. 2-Azoxypropane gave *NN'*-di-2-propylhydrazine (4-phenylthiosemicarbazide, m. p. 128°; Lochte *et al.*, *loc. cit.*, record m. p. 128°). Azoxy*cyclo*hexane gave *NN'*-di*cyclo*hexylhydrazine [*benzoyl* derivative, m. p. 101—102°, from alcohol (Found: C, 76·4; H, 9·5; N, 9·5. $C_{19}H_{28}ON_2$ requires C, 76·0; H, 9·3; N, 9·3%)].

(*c*) ω-Azoxy-*p*-chlorotoluene (150 mg.) was reduced in the presence of platinic oxide (80 mg.), alcohol (20 c.c.), and hydrochloric acid (0·2 c.c.; *d* 1·16). Reduction stopped when 11 mols. of hydrogen had been absorbed; the filtered solution was evaporated under reduced pressure to small volume and then treated with ether, giving a crystalline hydrochloride (145 mg.), m. p. 249—251°. The benzoyl derivative, crystallised from *n*-heptane, had m. p. 101—102° (Found: C, 77·6; H, 8·9; N, 6·1. Calc. for $C_{14}H_{19}ON$: C, 77·4; H, 8·8; N, 6·4%). The reduction product was thus hexahydrobenzylamine; Demjanow (*J. Russ. Phys. Chem. Soc.*, 1904, **36**, 166) records m. p. *ca.* 254° for the hydrochloride, and Skita (*Ber.*, 1923, **56**, 1014) gives m. p. 98° for the benzoyl derivative.

Reaction of Primary Azoxy-compounds with Hydrochloric Acid.—(*a*) 1-Azoxypropane (2 g.) and 8N-hydrochloric acid (40 c.c.) were heated together under reflux for 1 hour, the mixture being then homogeneous. The cooled solution was extracted with ether, evaporation of the ether yielding propionic acid, identified as the piperazine salt, m. p. 122—123°, and as the phenylhydrazide, m. p. 156—157°. The acidic aqueous layer was evaporated, giving *n*-propylhydrazine hydrochloride, which was identified by conversion into the *NN'*-dibenzoyl derivative, m. p. 127—128°. Stollé and Reichert (*J. pr. Chem.*, 1929, **122**, 344) give m. p. 128° for this compound (Found: N, 9·9. Calc. for $C_{17}H_{18}O_2N_2$: N, 9·9%). In a parallel experiment the *n*-propylhydrazine was determined iodimetrically (Found: 0·9 mol.).

(*b*) Azoxymethane and 8N-hydrochloric acid were heated together at 75° for 1 hour in a sealed tube, and the products isolated as described above. The formic acid was identified by reduction to formaldehyde which was detected by the reaction with chromotropic acid; the methylhydrazine was characterised as its *NN'*-dibenzoyl derivative, m. p. 141°. Iodimetric determination showed that 0·9 mol. of methylhydrazine was formed.

(*c*) (By Mr. J. N. Brough.) ω-Azoxy-*p*-chlorotoluene (1 g.), 12N-hydrochloric acid (24 c.c.) and alcohol (12 c.c.) were boiled together under reflux. After ¾ hour the mixture became homogeneous and then deposited colourless crystals, the amount of which decreased slowly as heating progressed. After 13 hours the reaction was terminated, the cooled mixture extracted with ether, and the ether evaporated, giving *p*-chlorobenzoic acid (410 mg.) which after sublimation had m. p. 235°, undepressed on admixture with authentic material. The aqueous acidic layer was filtered, giving a crystalline residue (226 mg.), m. p. *ca.* 212° (decomp.) (Found: C, 50·9; H, 4·0; N, 8·4; Cl, 31·6. $C_{14}H_{12}ON_2Cl_2$,HCl requires C, 50·7; H, 3·9; N, 8·4; Cl, 32·1%). When hydrolysed under reflux for 72 hours with concentrated hydrochloric acid and a little alcohol it gave *p*-chlorobenzoic acid (80%) and *p*-chlorobenzylhydrazine (70%); this compound is thus the *hydrochloride* of *N*-chlorobenzoyl-*N'*-*p*-chlorobenzylhydrazine. The free *base* had m. p. 148° (Found: C, 57·2; H, 4·4; N, 9·6. $C_{14}H_{12}ON_2Cl_2$ requires C, 57·0; H, 4·1; N, 9·5%).

Evaporation of the acid filtrate described above gave colourless crystals (371 mg.), m. p. *ca.* 160°, very soluble in water. The Schotten–Baumann method gave NN'-*dibenzoyl*-N-p-*chlorobenzylhydrazine*, m. p. 183—184° (Found: C, 69·3; H, 4·8; N, 7·6. $C_{21}H_{17}O_2N_2Cl$ requires C, 69·1; H, 4·7; N, 7·7%). A second portion of the *p*-chlorobenzylhydrazine was treated with phenyl *iso*thiocyanate, giving 2-p-*chlorobenzyl*-4-*phenylthiosemicarbazide*, m. p. 116—117°, from alcohol (Found: C, 57·6; H, 4·9; N, 14·6. $C_{14}H_{14}N_3SCl$ requires C, 57·6; H, 4·8; N, 14·4%). For comparison the same compound was also obtained by reducing *p*-chlorobenzaldehyde hydrazone with sodium amalgam and alcohol, and treating the resulting base with phenyl *iso*thiocyanate.

Reaction of Secondary Azoxy-compounds with Hydrochloric Acid.—(*a*) Azoxy*cyclo*hexane (500 mg.) and 8N-hydrochloric acid (10 c.c.) were heated together under reflux for 4 hours and the cooled solution was filtered. The residue was washed with ether, evaporation of the ether giving *cyclo*hexanone, identified as the 2 : 4-dinitrophenylhydrazone, m. p. 162°. The ether-insoluble material was recrystallised from light petroleum (b. p. 100—120°), giving dodecahydrotriphenylene (110 mg.), m. p. 232°. The acidic filtrate from the hydrolysis was shown by titration to contain 0·6 mol. of hydrazine. Evaporation of the main portion under reduced pressure, and treatment with sulphuric acid gave hydrazine sulphate, m. p. 252° (decomp.).

(*b*) 2-Azoxypropane (0·2 g.) and 12N-hydrochloric acid (2 c.c.) were heated in a sealed tube

at 100° for 20 hours and then cooled. The crystalline precipitate was identified as hydrazine hydrochloride by converting it into the sulphate. No acetone could be detected in the solution.

Hydrolysis of α-Azoxyisobutyric Acid.—The acid used was prepared according to Aston and Parker (*loc. cit.*). It was recrystallised from water and dried in a vacuum immediately before use. (*a*) A solution of the acid (100 mg.) in water was heated under reflux for 10 minutes and then titrated with 0·05N-sodium hydroxide (methyl-red) (Found: 0·49 equiv. of acid). The neutral solution was concentrated and treated with *S*-benzylthiuronium chloride, giving *S*-benzylthiuronium *iso*butyrate, m. p. 141—142°.

(*b*) The azoxy-acid (70 mg.) and water (5 c.c.) were heated in a sealed tube at 100° for 1 hour, then cooled and treated with a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid (50 c.c.). The acetone 2 : 4-dinitrophenylhydrazone (111 mg.), m. p. 126°, was collected and dried to constant weight in a vacuum (Found: 1·49 mols. of acetone).

(*c*) The nitrogen evolved when a solution of the azoxy-acid in water was heated in a current of air-free carbon dioxide was collected over 50% potassium hydroxide solution in a nitrometer (Found: N_2, 0·46 mol.).

(*d*) When the azoxy-acid and water were heated together gas was evolved containing carbon dioxide, and hydrazine was detected after the reaction was over by conversion into the sulphate, and was determined iodimetrically (Found: N_2H_4, 0·52 mol.).

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808. *The Photochemistry of Iodide Ions in Aqueous Solution.*

By TYSON RIGG and JOSEPH WEISS.

The photochemical formation of iodine and hydrogen from aqueous iodide solutions, by irradiation at 2000—2400 Å, has been investigated over a wide range of pH and iodide concentrations, and it has been found that the quantum yield depends markedly on both these factors. The following mechanism gives an adequate account of all the experimental facts:

$$(1a)\ (I^-,H_2O) + h\nu \longrightarrow (I^-,H_2O)^*,$$
$$(1b)\ (I^-,H_2O)^* \longrightarrow I + H + OH^-,$$
$$(2)\ I + H \longrightarrow HI$$

The dependence on pH is attributed to the intervention of hydrogen molecular ions, formed according to (3) $H + H^+ \rightleftharpoons H_2^+$ followed by (4) $H_2^+ + I^- \longrightarrow H_2 + I$, and (5) $2I \longrightarrow I_2$. There is also a second back-reaction, *viz.*, (6) $I_2 + H \longrightarrow HI + I$, which becomes important at higher iodine concentrations.

FRANCK and SCHEIBE (*Z. physikal. Chem.*, 1928, *A*, **139**, 22) were the first to interpret the ultra-violet absorption spectra of the halogen ions in solutions as electron-affinity spectra. This was subsequently taken up by Franck and Haber (*Sitzungber. Preuss. Akad. Wiss.*, 1931, 250), who suggested that the electron transfer from the ion (X^-,H_2O) to a water molecule in the hydration shell is represented by the process: $X^-,H_2O + h\nu \longrightarrow X + H + OH^-$.

Farkas and Farkas (*Trans. Faraday Soc.*, 1938, **34**, 1113) questioned some of these conclusions and suggested that the photochemical reaction takes place only by the transfer of the electron from the hydration shell to a hydrogen ion in the solution; this appeared to be confirmed by some observations of an increase in the quantum yield in acid solutions. On the other hand, for positive ions, such as the ferrous ion, according to these authors, the quantum yield should be independent of the hydrogen-ion concentration. However, the latter conclusion is not in agreement with the experimental evidence, for we have shown (*J. Chem. Physics*, 1952, **20**, 1194) that the photochemical formation of hydrogen and of ferric salt from aqueous solutions of ferrous ions is strongly dependent on the hydrogen-ion concentration, which could be interpreted on a quantitative basis by assuming the

intervention of the hydrogen molecular ion (H_2^+) in solution, formed by the association of a hydrogen atom with a hydrogen ion.

It has already been suggested that the pH dependence of the iodide-ion photolysis is also due to the formation and reaction of the hydrogen molecular ion (Weiss, *Nature*, 1950, **165**, 728). Hardly any quantitative data are recorded concerning the photochemistry of iodide ions *in the absence of atmospheric oxygen* except a few measurements by Farkas and Farkas (*loc. cit.*) and the qualitative observations by Butkow (*Z. Physik*, 1930, **62**, 71). We have, therefore, carried out a more detailed investigation, particularly with regard to the dependence of the quantum yield on pH and on the iodide-ion concentration.

FIGS. 1 and 2. *Dependence on* pH *of the quantum yield of iodine at constant light intensity* (5·025 × 10^{-5} *einstein/min.* × 100 *ml.*) *and time of irradiation* (6 *min.*).

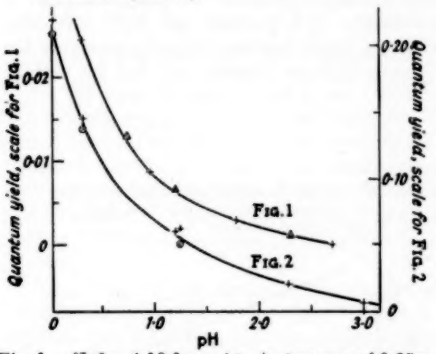
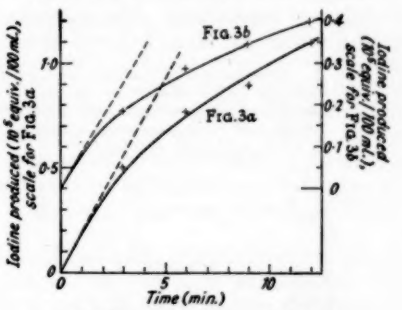


Fig. 1. $[I^-] = 4 \cdot 10^{-3}$ M. (△, *in presence of* 0·25M-Na_2SO_4.)
Fig. 2. $[I^-] = 2 \cdot 0$M. (+ *Iodine*, ○ *hydrogen determinations.*)

FIG. 3. *Dependence of iodine formation on time of irradiation at constant light intensity* (5·025 × 10^{-5} *einstein/min.* × 100 *ml.*).



(*a*) pH = 0·30, $[I^-] = 4 \cdot 10^{-3}$M;
(*b*) pH = 3·00, $[I^-] = 2 \cdot 0$M.

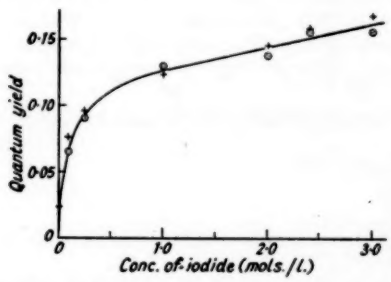


FIG. 4. *Dependence of the quantum yield of iodine* (+) *and hydrogen* (○) *on the iodide concentration at constant* pH ≃ 0·30, *constant light intensity* (5·025 × 10^{-5} *einstein/min.* × 100 *ml.*) *and constant time of irradiation* (6 *min.*).

All experiments were carried out under conditions of complete absorption of the incident light, which is the case even at relatively low iodide concentrations, on account of the high extinction coefficient of iodide ions in the region, 2000—2400 Å.

Figs. 1 and 2 represent the results obtained with $[I^-] = 4 \times 10^{-3}$M and $[I^-] = 2 \cdot 0$M respectively at different hydrogen-ion concentrations (for constant light intensity and time of irradiation); they show that there is a very marked dependence of the quantum yield on pH. Fig. 2 also shows the good agreement between the photochemically produced iodine and the simultaneously produced hydrogen, indicating clearly that there is no interference from any residual oxygen of the air: this is particularly important in the experiments with high iodide- and hydrogen-ion concentrations, as these solutions are very susceptible to autoxidation.

Figs. 3*a* and 3*b* show the dependence of the photochemically produced iodine on the time of irradiation, for constant light intensity for two pH's and for two iodide

concentrations. The time dependence is generally non-linear, which indicates the operation of some back reaction.

Similar results have been obtained at other pH and iodide concentrations. Some of the initial yields for constant light intensity are given in Table 1, and it is seen that the

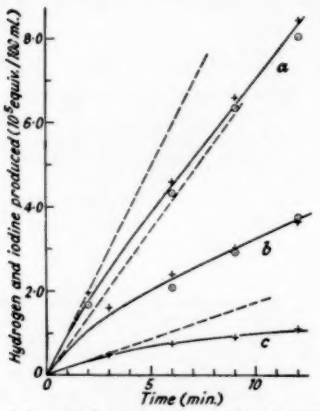
TABLE 1.

pH	Concn. of iodide, mol./l.	Initial rate* (mol./l. min.) × 10^5	pH	Concn. of iodide, mol./l.	Initial rate (mol./l. min.) × 10^5
1·78	0·004	0·316	3·00	2·0	0·95
0·95	,,	0·830	1·20	,,	4·46
0·30	,,	1·93	0·30	,,	10·0

* At constant light intensity.

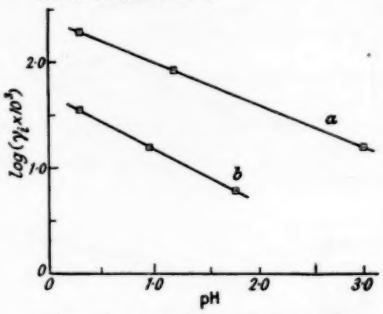
quantum yield increases markedly at the higher iodide concentrations. This is demonstrated more clearly by Fig. 4, which shows the dependence of the quantum yield on the iodide concentration in the range 0·004—3·0 mols./l. (at constant pH, light intensity, and time of irradiation). The quantum yield shows a rapid increase at comparatively low concentrations of iodide, followed by a relatively slow increase between 0·5 and 3·0 mols./l.

FIG. 5. *Dependence of iodine (+) and of hydrogen (⊙) formation on time of irradiation at constant light intensity (5·026 × 10^{-5} einstein/min. × 100 ml.) in* 1N-H_2SO_4 (pH ≃ 0·30).



(*a*) 2·0M-, (*b*) 0·1M-, (*c*) 4 × 10^{-3}M-*potassium iodide.*

FIG. 6. *Logarithmic plot of* initial *quantum yield* (γ_I) *against* pH, *for two different iodide concentrations.*



(*a*) 2·0M, (*b*) 4 × 10^{-3}M-*potassium iodide.*

Fig. 5 shows that the rate of iodine formation, under otherwise similar conditions, is greatly increased at higher iodide concentrations.

Discussion.—The modification of the theory as suggested by Farkas and Farkas (*loc. cit.*) introduces into the photochemistry of iodide ions a dependence of the quantum yield on the pH. These authors suggested that the actual chemical process is initiated by reaction of the "excited" ions with hydrogen ions which can be represented by : $I^- + h\nu \longrightarrow (I^-)^*$, followed by $(I^-)^* + H^+ \longrightarrow I + H$, with the following process of deactivation : $(I^-)^* \longrightarrow I^- +$ energy. This mechanism would lead to the following expression :

$$\text{quantum yield} = \text{const.} \times [H^+]/(1 + \text{const.} \times [H^+])$$

according to which the quantum yield should be independent of the iodine concentration and should approach *unity* with increasing hydrogen-ion concentration. This expression is, however, not in agreement with the experimental results.

On the other hand, if one introduces H_2^+ into the mechanism, the experimental results can be satisfactorily interpreted on the basis of a photochemical primary process somewhat similar to that suggested by Franck and Haber (*loc. cit.*).

Derivation of the Kinetics.—The following elementary processes have to be considered :

light absorption: $(I^-,H_2O) + h\nu \longrightarrow (I^-,H_2O)^*$ (I_a = light absorbed per unit of time) . (1*a*)

" dissociation " of the " excited ion ": $(I^-,H_2O)^* \longrightarrow I + H + OH^-$ . . . (1*b*)

$$I + H \xrightarrow{k_2} HI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$H + H^+ \underset{k_3'}{\overset{k_3}{\rightleftarrows}} H_2^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)(3')$$

$$I^- + H_2^+ \xrightarrow{k_4} I + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$2I \xrightarrow{k_5} I_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$I_2 + H \xrightarrow{k_6} HI + I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$I_2 + I^- \rightleftarrows I_3^-$ (equilibrium constant $K_T \simeq 1{\cdot}36 \times 10^{-3}$ at 25°) . . (7)

In the case of positive ions, *e.g.*, ferrous, we have concluded that most of the excited ions undergo a process of deactivation. This apparently does not apply to the excited iodide ions, where the electron transferred to the hydration shell seems to have a much greater tendency to " split " a water molecule according to (1*b*), which is similar to the primary process suggested by Franck and Haber. However, the intermediate formation of an " excited " iodide ion is made probable by the recent considerations by Platzman and Franck (personal communication) concerning the absorption spectrum of iodide ions in solution.

According to our findings, the reason why the quantum yield is relatively low here is not the deactivation of the excited iodide ions, but the very efficient back-reaction (2) between the hydrogen and the iodine atoms, which is probably enhanced by the Franck–Rabinovitch " cage effect."

The experimental results indicate that at higher iodine concentrations a second back-reaction (6) between molecular iodine and hydrogen atoms has to be taken into account. This reaction should be relatively less important at higher iodide concentrations, on account of the formation of tri-iodide ions, according to the equilibrium (7) from which the " true " concentration of $[I_2]$ in terms of the total (*analytical*) concentration of iodine (I_2) is given by :

$$[I_2] = (I_2)K_T/(K_T + [I^-]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

From equations (1)—(6) one obtains for the stationary state of the unstable intermediates the equations :

$$d(I^-,H_2O)^*/dt = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (II\,a)$$

$$d(I)/dt = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (II\,b)$$

$$d(H)/dt = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (II\,c)$$

$$d(H_2^+)/dt = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (II\,d)$$

This leads to the equation

$$I_a - k_2[H][I] - k_5[I]^2 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (III\,a)$$

Substituting for [H] from the above equations for the stationary state, one obtains

$$[H] = (k_5/\Gamma)[I]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (III\,b)$$

where

$$\Gamma = \{k_3k_4[H^+][I^-]/(k_3' + k_4[I^-])\} + k_6[I_2] \quad . \quad . \quad . \quad . \quad (III\,c)$$

and with equation (III*a*) this gives

$$I_a - k_5[I]^2 - (k_2k_5/\Gamma)[I]^3 = 0 \quad . \quad . \quad . \quad . \quad . \quad (III\,d)$$

Thus one obtains for the rate of formation of molecular iodine (or hydrogen) :

$$d(I_2)/dt = d(H_2)/dt = k_5[I]^2 - k_6[H][I_2]$$
$$= k_5[I]^2\{1 - k_6K_T(I_2)/\Gamma(K_T + [I^-])\} \quad . \quad . \quad (IV\,a)$$

As shown in Figs. 3*a* and 3*b*, in general, there is a non-linear dependence of the yield on the time of irradiation (for constant light intensity).—However, the first term in (IV*a*) would normally lead to a linear dependence as the pH and $[I^-]$ can be regarded as practically constant. Thus it appears that, in order to account for the experimental facts, it is necessary to take into account a back-reaction. Reaction (6) meets all the necessary requirements. The treatment of the complete equation (IV*a*) leads to complicated expressions; therefore, in the following discussion mainly the *initial* yields have been considered.

In the calculation of the stationary iodine atom concentration from (III*d*) it is obvious that only the cubic term depends on the hydrogen-ion concentration, whereas the quadratic term by itself would lead to a rate which increases only very slowly with increasing acidity and, initially, would be completely independent of pH.

On the other hand, the strongest dependence on pH is obtained if one neglects the quadratic term in (III*d*), *i.e.*, if

$$k_2[I] \gg \Gamma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (V)$$

which, for the *initial* formation of iodine, leads to the rate equation

$$d(I_2)/dt|_i \simeq k_5[I]^2 \simeq k_5(I_a\Gamma/k_2k_5)^{2/3} \quad . \quad . \quad . \quad . \quad . \quad . \quad (VI*a*)$$

and for the initial quantum yield (γ_i) from (VI*a*) and (III*d*)

$$\gamma_i = (1/I_a)d(I_2)/dt \propto k_5\{k_3k_4[H^+][I^-]/(k_3' + k_4[I^-])\}^{2/3} \quad . \quad . \quad . \quad (VI*b*)$$

The dependence of the quantum yield (γ) on the pH at constant light intensity and time of irradiation is shown by Figs. 1 and 2, for two widely different iodide concentrations.

For a more quantitative comparison the *initial* yields, at constant iodide concentration, for different pH have been taken from Table 1, and in Fig. 6 $\log \gamma_i$ is plotted against pH. From a generalisation of (VI*a*) it follows that

$$\gamma_i \propto [H^+]^n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (VII*a*)$$

with $0 \leqslant n \leqslant 0{\cdot}66$, where the lower limit would correspond to the case where the inequality (V) is reversed. Thus

$$d \log \gamma_i/d\,pH = -n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (VII*b*) .$$

Experimentally one finds from Fig. 6:

$$d \log \gamma_i/d\,pH = -0{\cdot}52 \pm 0{\cdot}04 \text{ (for } [I^-] = 4 \times 10^{-3}\text{M}) = -0{\cdot}40 \pm 0{\cdot}04 \text{ (for } [I^-] = 2{\cdot}0\text{M})$$

which are both nearer the maximum value of $-0{\cdot}66$. It is clear that if condition (V) does not hold very well, the cubic equation (III*d*) would have to be solved completely for a more detailed discussion. This is, however, not possible without some independent knowledge of some of the rate constants involved.

As the experimental error in the actual determination of the *initial* yields is certainly not more than $\pm 10\%$, the slopes in Fig. 6 are accurate to within the limits stated.

The fact that the slope (n) decreases with increasing iodide concentration follows immediately from equation (III*d*), as Γ generally increases with increasing iodide concentration and thus the cubic term becomes less important relative to the quadratic term, which is independent of pH. Although the iodide concentration in the two cases considered above differs by a factor of 500, the decrease in the slope at the higher iodide concentration is relatively small; this can also be deduced from equations (III*d*) and (III*c*), which show that Γ will increase only relatively *slowly* with increasing iodide-ion concentration.

Some further semiquantitative confirmation of the theory can be obtained from a consideration of the initial rates at different iodide concentrations at constant pH. There is a marked increase of the initial yield with increasing iodide concentration, as shown by Fig. 5 which represents the yield for constant pH and constant time of irradiation, over a wide range of iodide concentration; at low concentrations there is a rapid increase of the yield which, however, increases only relatively slowly beyond a certain iodide concentration. The general character of the curve is well represented by an equation of the form

$$\gamma_i \simeq \{K_1[I^-]/(1 + K_2[I^-])\}^n \quad . \quad . \quad . \quad . \quad . \quad . \quad (VIII)$$

which is suggested by the theoretical equation (VI*b*), where K_1 and K_2 are independent of the iodide concentration.

However, in the theoretical evaluation of the experiments at high iodide concentrations, there is also the difficulty that there is a very considerable change in the ionic strength, and for a more quantitative treatment some definite information regarding the activity coefficients would also be required. Furthermore, it must be borne in mind that at the higher iodide concentrations practically complete light absorption occurs in a very thin layer, and this may also modify somewhat the course of the reaction. Nevertheless, the initial yields of the experiments given in Fig. 4 are fairly well represented by a relation of the type of equation (VIII), the upper limit being taken for the exponent, as shown by the data in Table 2. Although these figures are primarily of qualitative significance, on the whole there is satisfactory agreement between the theory and the experimental results.

TABLE 2.

Concn. of iodide, mols./l.	Initial rate * $[d(I_2)/dt]_i$, (mols./l. × min.) × 10^5: Found	Calc. from $\{2 \times 10^{-5}\,[I^-]/(1 + 20[I^-])\}^{\frac{1}{2}}$
2·0	10·0	9·85
0·1	7·0	7·58
0·004	1·8	1·76

* At constant light intensity.

EXPERIMENTAL

The source of radiation was a low-pressure mercury discharge tube of about 500 watts, used in conjunction with a voltage stabiliser (Ferranti). Unfiltered radiation was used under conditions of complete absorption. The apparatus was on conventional lines. A spherical silica flask, filled with triply distilled water, was used as a condenser. In this way, and with a small centrifugal blower, the temperature in the reaction vessel could be kept constant at 20° ± 1°.

Actinometry.—The total light output in the ultra-violet region was measured actinometrically by means of chloroacetic acid. This was chosen since its absorption spectrum shows a good overlap with that of iodide ions in aqueous solutions, and the error involved should not amount to more than about 10% which was adequate for the purpose of the present investigation.

The value 0·62 ± 0·04 used for the quantum efficiency of chloroacetic acid photolysis is due to Kuechler and Pick (*Z. physikal. Chem.*, 1940, *B*, **45**, 116), who carried out a very careful investigation of this reaction. The light absorbed by the solution was $5{\cdot}025 \times 10^{-5}$ einstein/(min. × 100 ml.).

Preparation of Solutions.—The water used was ordinary distilled water redistilled from permanganate and then from dilute phosphoric acid. It was boiled out in a stream of carbon dioxide, and after cooling in the gas stream it could be syphoned out of its container as required.

The procedure adopted in making up the solutions was as follows. Some of the carbon dioxide-saturated water was acidified with sulphuric acid to the extent required, and 100 ml. were introduced into the reaction vessel which was already *in situ* on the evacuation apparatus. A fairly vigorous stream of carbon dioxide was then passed through the solution for some minutes to sweep out all the air, and then pumped out with an oil-pump and a liquid-air trap.

In the experiments with dilute solutions, the potassium iodide was introduced into the reaction vessel immediately before pumping out. The method of preparing the concentrated solutions (up to 3M) was somewhat different: the requisite amount of solid potassium iodide was dropped *via* a specially designed orifice into the acidified water in the vessel after deaeration (carbon dioxide bubbling through continuously), and the solution was then immediately pumped out as above. In this way, it was found possible to prepare even 3M-solutions of potassium iodide in 1M-sulphuric acid without any measurable autoxidation occurring.

De-aeration of the Solutions.—All experiments were carried out in evacuated solutions. The first stage of evacuation is described in the preceding section, a " Hyvac " oil-pump being used to pump out the gas *via* a liquid-air trap. More carbon dioxide was then admitted, and the vessel again pumped out. Evacuation was finally completed and checked on the gas-analysis apparatus where the solutions were evacuated by means of a Toepler pump. The vapour phase in equilibrium with the solutions was also tested for oxygen by means of a trypaflavine gel and it was shown that the oxygen pressure did not exceed 10^{-5} mm. Hg. No effects due to residual oxygen could be observed in any of the experiments after using the above procedure.

Quantitative Estimations.—In the experiments with dilute solutions (4×10^{-3}M) the vessel was cooled in ice and filled with carbon dioxide after irradiation, the contents being quickly titrated in a slow stream of carbon dioxide with thiosulphate and starch indicator. In the more concentrated solutions the yield of hydrogen and iodine was large enough to enable the former to be measured also. Up to 1 ml. of gas was obtained in these experiments and was shown to be pure hydrogen by diffusion through a palladium tube after no contraction could be observed on passage over a heated platinum spiral. After the gas had been removed, the vessel was filled with carbon dioxide and the contents were titrated with thiosulphate.

In the determination of the small amounts of iodine in the presence of more than 0·1M-potassium iodide some difficulty was experienced, since a purplish-red colour was produced with the starch indicator instead of the usual intense blue colour. This red iodine complex seemed to react only slowly with the thiosulphate, but reliable results could be obtained by adding initially an excess of thiosulphate and back-titrating with iodine solution.

Blank experiments were always carried out but no detectable amounts of iodine could be observed under the conditions described above. This is also confirmed by the fact that, in those cases where hydrogen and iodine determinations were carried out, the agreement was always satisfactory, as will be seen from Figs. 2, 4, and 5.

Normally, the accuracy of the iodine titrations was $\pm 0{\cdot}5\%$, but in the 2M-iodide solutions, where the difficulties described above arise, the titration is accurate only within $\pm 5\%$. However, in these solutions the hydrogen measurements are correspondingly more accurate ($\pm 2\%$) owing to the increased yields.

All reagents used in the course of this investigation were of " AnalaR " grade.

We thank the Chemical Society for a grant towards the purchase of some of the apparatus, and one of us (T. R.) thanks the Cumberland Education Committee for a maintenance grant.

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809. *Structural Chemistry of the Alkoxides. Part II.* Tertiary Alkoxides of Silicon, Titanium, Zirconium, and Hafnium.*

By D. C. BRADLEY, R. C. MEHROTRA, and W. WARDLAW.

The tertiary alkoxides $M(O{\cdot}CMe_nEt_{3-n})_4$, $M(O{\cdot}CMe_2R)_4$, and $M(O{\cdot}CMeEtPr^i)_4$, where M = Ti or Zr; n = 0, 1, 2, or 3; and R = Me, Et, Pr^n, Pr^i, or Bu^t, have been prepared. Ebullioscopic measurements show that these compounds are monomeric. Vapour-pressure measurements on the lower tertiary alkoxides show that boiling points and latent heats increase with molecular size but entropies of vaporisation show little variation. A comparison of isomeric tertiary alkoxides reveals the effect of chain branching on volatility. Most titanium tertiary alkoxides are less volatile than their zirconium analogues while hafnium *tert.*-amyloxide is more volatile than the zirconium derivative. Hence the surprising order of volatilities, Hf>Zr>Ti, is found for the *tert.*-amyloxides. The position of silicon in this series is discussed.

IN Part I * of this series it was established that the volatility of the amyloxides of titanium and zirconium depends on the structure of the amyl group. It was suggested that strong intermolecular bonding involving the central atom and oxygen is responsible for the low volatility of the straight-chain amyloxides, whilst in the *tert.*-amyloxides the screening effect of the branched amyloxide groups opposes intermolecular association and leads to greater volatility. Thus the tertiary compound is the only monomer in the zirconium series and its boiling point is close to that of the titanium analogue. It seemed reasonable to suppose that all tetra-*tert.*-alkoxides of titanium and zirconium would be monomeric, thus allowing a study to be made of the influence of molecular size on volatility whilst an examination of isomeric higher tertiary alkoxides should decide whether structural effects are still important. Further the tertiary alkoxides were considered to be suitable for

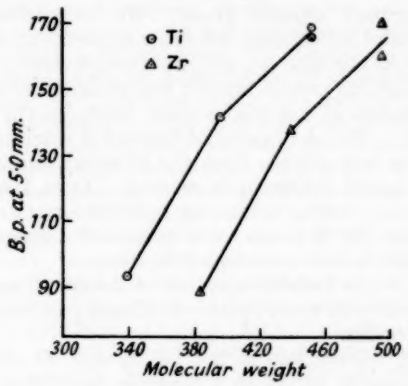
* Part I, *J.*, 1952, 2027.

investigating the influence of the central atom on volatility. Accordingly the series of alkoxides $M(O{\cdot}CMe_nEt_{3-n})_4$, $M(O{\cdot}CMe_2R)_4$, and $M(O{\cdot}CMeEtPr^i)_4$ were prepared and examined for the compounds where M = Ti or Zr, n = 0, 1, 2, or 3, and R = Me, Et, Pr^n, Pr^i, or Bu^t.

In ebullioscopic experiments all the compounds measured were found to be monomeric. Boiling points were measured at several pressures between 0·1 and 10·0 mm. Hg for the more volatile compounds and in all cases the data fitted straight lines of the form $\log p_{mm} = a - b/T$ in the pressure range 2—10 mm. The values for the constants a and b are listed in Table 1 together with boiling points (under 5·0 mm. pressure), latent heats of vaporisation (L_v) and entropies of vaporisation at 5·0 mm. pressure ($\Delta S_{5\cdot0}$).

The boiling points from Table 1 are plotted against molecular weights in the Figure, and the boiling points of the higher alkoxides are given in Table 2.

It is seen that the boiling points do not increase linearly with molecular weights. Moreover, the three tertiary heptyloxides gave boiling points in the order $M(O{\cdot}CMeEtPr^i)_4$>



$M(O{\cdot}CEt_3)_4$>$M(O{\cdot}CMe_2Bu^t)_4$, showing clearly that even in the monomeric tertiary alkoxides the effect of chain branching is still significant. An interesting point that emerges from Table 1 is that although the latent heats increase with molecular size the entropies

TABLE 1.

Alkoxide	B. p.	L_v (kcal./mole)	a	b	$\Delta S_{5\cdot0}$ (cal. mole^{-1} deg.$^{-1}$)
$Ti(O{\cdot}CMe_3)_4$	93·8	14·5	9·34	3170	39·5
$Zr(O{\cdot}CMe_3)_4$	89·1	15·2	9·90	3330	42·0
$Ti(O{\cdot}CMe_2Et)_4$	142·7	16·7	9·46	3640	40·0
$Zr(O{\cdot}CMe_2Et)_4$	138·4	16·3	9·34	3550	39·5
$Ti(O{\cdot}CMeEt_2)_4$	170·4	19·0	10·1	4170	43·0
$Zr(O{\cdot}CMeEt_2)_4$	171·4	19·0	10·1	4170	43·0
$Ti(O{\cdot}CMe_2Pr^n)_4$	167·0	19·5	10·4	4270	44·0
$Zr(O{\cdot}CMe_2Pr^n)_4$	161·6	19·0	10·2	4140	44·0

TABLE 2.

Alcohol	Ti alkoxide	Zr alkoxide	Alcohol	Ti alkoxide	Zr alkoxide
$Pr^iMe_2C{\cdot}OH$	147°/0·5	133°/0·1	$Bu^tMe_2C{\cdot}OH$	163°/0·5	168°/0·5
$Et_2C{\cdot}OH$	180°/0·5	180°/0·4	$Pr^iEtMeC{\cdot}OH$	197°/1·0	194°/0·7

of vaporisation are sensibly constant (42 ± 2·5 cal. mole^{-1} deg.$^{-1}$) irrespective of whether the central atom is titanium or zirconium, thus emphasising the structural similarity of these compounds.

For a given tertiary alkoxide it is seen that there is little difference in the boiling points of the titanium and the zirconium derivative. In fact it appears that the titanium analogue

often has the higher boiling point. Moreover, fractional distillation of a mixture of the tetra-*tert.*-amyloxides of zirconium and hafnium revealed that the hafnium derivative was slightly the more volatile. From general considerations it would be reasonable to expect that the order of volatilities for the tetra-*tert.*-alkoxides of silicon and the Group IVA elements would be $Si(OR)_4>Ti(OR)_4>Zr(OR)_4>Hf(OR)_4>Th(OR)_4$. However, it appears that for the *tert.*-amyloxides the actual order of volatilities is Hf>Zr>Ti. The position of silicon in this series is thus of exceptional interest particularly in view of the fact that the preparation of a tetra-*tert.*-alkoxide of this element has not yet been reported. Miner, Bryan, Holysz, and Pedlow (*Ind. Eng. Chem.*, 1947, **39**, 1368) described the preparation of $SiCl_3{\cdot}OR$, $SiCl_2(OR)_2$, and $SiCl(OR)_3$, but not $Si(OR)_4$, where R = Bu^t or CMe_2Et, from reactions involving silicon tetrachloride, pyridine, and tertiary alcohol, and this result has recently been confirmed by Gerrard and Woodhead (*J.*, 1951, 519). In addition, Miner *et al.* (*loc. cit.*) demonstrated that the tri-*tert.*-butoxychlorosilane $SiCl(OBu^t)_3$ can be converted into the mixed alkoxide $Si(OBu^t)_3{\cdot}OBu^n$. Thus the reactivity of the chlorine in $SiCl(OR)_3$ is beyond doubt and it appears that steric considerations prevent the introduction of the fourth tertiary alkoxide group. We have attempted to prepare silicon tertiary alkoxides by alcohol interchange involving tetraethoxysilane but without success. In our previous communication (*loc. cit.*) attention was drawn to the remarkable shielding effect of four tertiary alkoxide groups around the titanium or zirconium atom and it is possible that the small radius of the silicon atom precludes the formation of tetra-*tert.*-alkoxides of this element. The chief point of interest is whether the tetra-*tert.*-alkoxides of silicon will be more or less volatile than the titanium analogues. From the boiling points of $Si(OBu^s)_2(OBu^t)_2$ and $Si(OBu^s)_4$ (Woodhead, Thesis, London, 1950), it is deduced that $Si(OBu^t)_4$ should have a boiling point close to 60°/0·5 mm., since the boiling points of the corresponding titanium (65°/0·5 mm.) and zirconium compounds (63°/0·5 mm.) show that there is probably little variation through the series.

Interest now moves to the heaviest element of Group IV since the size and electropositive nature of the thorium atom may play a dominant part in determining the properties of thorium tetra-*tert.*-alkoxides.

The unusual volatility relationship in the Ti, Zr, and Hf series of tertiary alkoxides reported in this communication serves as a reminder that other examples are known of compounds having "anomalous" boiling points (*e.g.*, CCl_4 and $SiCl_4$; $InCl_3$ and $TlCl_3$) and that no convincing explanation has as yet been given for these phenomena.

Experimental

Materials.—Silicon, titanium, and zirconium tetrachlorides were commercial products and used without further purification. 1-Ethyl-1-methylpropanol was prepared from ethyl methyl ketone and ethylmagnesium bromide. 1 : 1 : 2-Trimethyl- and 1 : 1 : 2 : 2-tetramethyl-propanol were obtained from reactions involving acetone and the appropriate Grignard reagents. 1-Ethyl-1 : 2-dimethylpropanol was prepared from ethyl methyl ketone and *iso*propylmagnesium bromide. 1 : 1-Diethylpropanol was obtained from ethyl carbonate and ethylmagnesium bromide. Other alcohols used were the purest commercial products available. With the exception of *tert.*-butyl alcohol all the tertiary alcohols were azeotropically dried and carefully purified by fractionation through a column (70 cm.) packed with Fenske helices. *tert.*-Butyl alcohol was first dried with quicklime and then distilled over sodium. Pyridine ("AnalaR") was dried over barium oxide and distilled. The lower alcohols and solvents were dried and purified by the methods previously described (Bradley and Wardlaw, *J.*, 1951, 280; Bradley, Mehrotra, and Wardlaw, Part I, *loc. cit.*).

Analytical Methods.—Silicon, titanium, zirconium, methoxide, ethoxide, or *iso*propoxide were determined as previously described. In the mixed alkoxides ethoxide could be determined in the presence of *tert.*-butoxide without modification of the normal method, but for methoxide in the presence of *tert.*-butoxide an empirical method was used. Carbon and hydrogen analyses were by Messrs. Weiler and Strauss (Oxford) whom we thank for their co-operation.

Molecular Weights.—Molecular weights (see Table) were determined ebullioscopically in benzene (Bradley, Mehrotra, and Wardlaw, *loc. cit.*). One apparatus gave an ebullioscopic constant of 31·5 whereas a second gave 29·8. Determinations in the latter apparatus are marked by an asterisk.

Alkoxide	Range of *m* (g.)	No. of determns.	Benzene (c.c.)	$\Delta T/m$ (°/g.)	*M*, found	*M*, calc.
$Ti(O{\cdot}CMe_3)_4$ *	0·169—1·644	5	37·6	0·228	347 †	340·3
$Zr(O{\cdot}CMe_3)_4$ *	0·084—0·844	5	37·5	0·208	381	383·7
$Ti(O{\cdot}CMe_2Et)_4$	0·222—1·357	5	34·0	0·229	404	396·5
$Zr(O{\cdot}CMe_2Et)_4$	0·555—2·037	4	35·9	0·193	454	439·8
$Ti(O{\cdot}CMeEt_2)_4$	0·177—1·506	5	36·3	0·183	474	452·5
$Zr(O{\cdot}CMeEt_2)_4$	0·104—1·656	5	35·6	0·172	514	496
$Zr(O{\cdot}CEt_3)_4$	0·143—1·563	6	35·8	0·1655	532	552

† Cullinane *et al.* (*J. Appl. Chem.*, 1951, **1**, 400) found *M*, 315 (cryoscopic in benzene).

Boiling Points.—B. p.s at low pressures were measured in the apparatus described in Part I (*loc. cit.*). B. p.s over a range of pressures were determined in a special all-glass apparatus consisting of a flask (10 c.c.) joined through a semimicro-Claisen head to a total condensation variable take-off stillhead. Thus b. p.s under conditions of total reflux were measured and the purity of the alkoxide could be checked by collecting fractions. The rate of reflux, size of capillary leak, and temperature difference between heating-bath and thermometer pocket were standardised to be the same in each experiment. Pressures were read on a mercury manometer.

Preparation of Alkoxides.—Except for the *tert.*-butoxides the alkoxides were prepared by alcohol interchange involving the *iso*propoxide and the appropriate higher alcohol. Titanium tetra-*tert.*-butoxide was prepared from the tetrachloride by Cullinane, Chard, Price, and Millward's method (*J. Soc. Chem. Ind.*, 1950, **69**, S38). Although zirconium tetra-*tert.*-butoxide was obtained by Bradley and Wardlaw (*loc. cit.*) the yields were small and hence other methods were investigated. Alcohol interchange involving either the tetramethoxide or tetraethoxide of zirconium gave only mixed alkoxides but the tetra-*tert.*-butoxide was obtained by thermal disproportionation of the mixed alkoxide. The *iso*propoxides of titanium and zirconium were prepared by the methods described in Part I.

Titanium tetra-tert.-*butoxide.* Titanium tetrachloride (55 g.) was added dropwise with constant stirring to *tert.*-butyl alcohol (167 g.) and pyridine (55 g.) in benzene (150 c.c.). Ammonia was passed into the mixture until the products had cooled to room temperature. After filtration and evaporation of the filtrate the final product distilled as a colourless liquid (78 g.), b. p. 107—108°/10 mm. (Found: Ti, 14·0. Calc. for $C_{16}H_{36}O_4Ti$: Ti, 14·1%). B. p.s: 64·5°/0·4, 69·5°/0·8, 81°/2·0, 91°/4·2, 96°/5·7, 100°/7·0, 106°/9·0, and 109°/11·0 mm.

Zirconium tetra-tert.-*butoxide.* (*a*) Zirconium tetramethoxide was prepared by the action of methanol (106 g.) on zirconium *iso*propoxide (32·4 g.) in benzene (77 g.). After 4 hours' refluxing the gelatinous precipitate was filtered off and refluxed with more methanol (150 g.) for 6 hours. The solid product was dried for 2 hours at 160°/0·1 mm. (Found: Zr, 41·3. Calc. for $C_4H_{12}O_4Zr$: Zr, 42·4%). To the foregoing product (11·0 g.) was added *tert.*-butyl alcohol (120 g.) and benzene (500 c.c.); the mixture was boiled and volatile products were fractionated through a column (70 cm.) packed with Fenske helices. The white solid slowly dissolved and the b. p. of the distillate under total reflux fell to 59° (b. p. of methanol–benzene azeotrope). During 2 hours distillate (10 c.c.) boiling between 59° and 64° was collected, then the b. p. rose rapidly to 72°. Fractionation was continued at a high reflux ratio for 12 hours until pure benzene was collected. The clear solution (30 c.c.) deposited crystals (9·8 g.) (Found: Zr, 27·8%). The solid product was recrystallised from benzene (20 c.c.) and proved to be a mixed alkoxide (6·0 g.) [Found: Zr, 27·7; MeO, 11·1. Calc. for a mixture of $Zr(OBu)_3{\cdot}OMe$ (4 mols.) and $Zr(OMe)_2(OBu)_2$ (1 mol.): Zr, 27·4; MeO, 11·2%]. The mixed alkoxide (5·4 g.) was heated at 8 mm., melting at 60—70°, and boiling at 180° to give a distillate, b. p. 100°/8 mm. Heating was continued for 4 hours at 220°, after which volatile material was collected at 1 mm. The white residue (1·4 g.) showed no loss in weight after prolonged heating at 220° (Found: Zr, 35·1, MeO, 33·4%; MeO : Zr, 2·8) and appeared to be mainly zirconium mono-*tert.*-butoxide trimethoxide. The volatile product was redistilled and gave a colourless mobile liquid (2·6 g.), b. p. 86°/4 mm. (Found: Zr, 23·9. Calc. for $C_{16}H_{36}O_4Zr$: Zr, 23·8%). The disproportionation appears to take the course $3Zr(OBu^t)_3{\cdot}OMe \longrightarrow 2Zr(OBu^t)_4 + Zr(OMe)_3{\cdot}OBu^t$.

(*b*) To zirconium tetraethoxide [30 g.; prepared from $(C_5H_6N)_2ZrCl_6$ by the method of Bradley, Halim, Sadek, and Wardlaw, *J.*, 1952, 2023] were added *tert.*-butyl alcohol (54 g.) and benzene (400 c.c.), and the mixture was fractionally distilled (90-cm. column). During the first 2 hours benzene–ethanol azeotrope (29 g., 50%) was collected and thereafter subsequent interchange was very slow, the b. p. of distillate rising from 69° to 73°. Removal of solvent left a very viscous liquid (36·7 g.) which was caused to disproportionate at 180°/0·4 mm. for several hours until no more volatile product was collected. A very viscous residue remained

(27·9 g.) (Found : Zr, 28·0%). After some weeks this residue gave more volatile products when heated at a higher temperature (220°) and pressure (8·5 mm.). When disproportionation had ceased the viscous residue was itself distilled (16·1 g.; b. p. 195°/1·4 mm.) (Found : Zr, 29·0%). This compound suffered no further disproportionation when heated at 240°/8·5 mm. and was redistilled, giving a very viscous distillate (14·6 g.; b. p. 190°/1·5 mm.) (Found : Zr, 28·9; EtO, 25·0%; EtO : Zr, 1·75). This remarkably stable mixed alkoxide of zirconium is evidently mainly $Zr(OEt)_2(OBu^t)_2$. The combined volatile products (13·2 g.) were shown by distillation (b. p. 100·5°/8·5 mm.) to be zirconium tetra-*tert.*-butoxide.

B. p. of $Zr(OBu^t)_4$: 55°/0·2, 72°/1·1, 74·5°/1·5, 79·5°/2·5, 85·5°/4·0, 92·5°/6·0, 100·5°/8·5, 102°/10, and 104°/12 mm.

Titanium tetra-(1 : 1-*dimethylpropoxide*). Prepared as in Part I, this had b. p.s 109·5°/0·3, 114·5°/0·6, 126°/2·0, 138°/4·0, 150°/7·0, 154°/8·7, and 157·5°/10·0 mm.

Zirconium tetra-(1 : 1-*dimethylpropoxide*). Prepared as in Part I, this had b. p.s 93·0°/0·1, 123°/2·0, 134°/4·0, 144°/6·7, 145·5°/7·5, and 153°/10·0 mm.

Titanium tetra-(1-*ethyl*-1-*methylpropoxide*). Titanium *iso*propoxide (3·5 g.) in benzene (80 c.c.) was heated with 1-ethyl-1-methylpropanol (7·3 g.; b. p. 122°/760 mm.), and the benzene–propan-2-ol azeotrope collected by fractionation. After the removal of solvent the new *alkoxide* was distilled and gave a colourless liquid (5·0 g.), b. p. 154°/2 mm. (Found : Ti, 10·65; C, 64·1; H, 11·5. $C_{24}H_{52}O_4Ti$ requires Ti, 10·6; C, 63·7; H, 11·6%). B. p.s : 139°/0·8, 149°/1·5, 154°/2·0, 161°/3·3, 166°/4·0, 172°/5·6, 178·5°/7·5, 184°/9·8, and 187°/11·0 mm.

Zirconium tetra-(1-*ethyl*-1-*methylpropoxide*). From the reaction involving zirconium *iso*propoxide (7·5 g.) and 1-ethyl-1-methylpropanol (11·2 g.) in benzene (70 c.c.) the benzene–propan-2-ol azeotrope (24 c.c.) was collected. After removal of solvent the new *alkoxide* was twice distilled and gave a colourless mobile liquid (8·0 g.), b. p. 150°/1·2 mm. (Found : Zr, 18·7; C, 56·8; H, 11·2. $C_{24}H_{52}O_4Zr$ requires Zr, 18·4; C, 58·1; H, 10·6%). B. p.s : 150°/1·2, 154°/1·7, 161·5°/3·0, 171°/5·0, 178·5°/7·0, 180°/7·5, 186°/9·8, and 186·5°/10·0 mm.

Titanium tetra-(1 : 1-*dimethylbutoxide*). Titanium *iso*propoxide (9·2 g.) in benzene (70 c.c.) was caused to react with 1 : 1-dimethylbutanol (15 g.; b. p. 123°/757 mm.) and the benzene–propan-2-ol azeotrope removed by fractionation. Removal of solvent left the new *alkoxide* which on distillation gave a colourless mobile liquid (13·5 g.), b. p. 141°/0·8 mm. (Found : Ti, 10·5. $C_{24}H_{52}O_4Ti$ requires Ti, 10·6%). B. p.s : 141°/0·8, 146°/1·5, 154°/2·5, 162°/4·0, 165·5°/4·8, 174°/7·0, 175°/7·5, and 181°/10·5 mm.

Zirconium tetra-(1 : 1-*dimethylbutoxide*). The reaction between zirconium *iso*propoxide (8·4 g.) and 1 : 1-dimethylbutanol (10·0 g.) was carried out in benzene (70 c.c.) in the usual way. The new *alkoxide* was a yellow mobile liquid (8·0 g.), b. p. 133°/0·7 mm. (Found : Zr, 18·3. $C_{24}H_{52}O_4Zr$ requires Zr, 18·4%). B. p.s : 133°/0·7, 137°/1·0, 144°/1·7, 151°/2·8, 157°/4·0, 164°/5·6, 171°/8·0, and 176°/10·0 mm.

Titanium tetra-(1 : 1 : 2-*trimethylpropoxide*). From the reaction involving titanium *iso*propoxide (7·9 g.) and 1 : 1 : 2-trimethylpropanol (12·1 g.; b. p. 119°/740 mm.) in benzene (60 c.c.) the new *alkoxide* was obtained as a colourless mobile liquid (10·4 g.), b. p. 147°/0·5 mm., 153°/1·0 mm. (Found : Ti, 10·5. $C_{24}H_{52}O_4Ti$ requires Ti, 10·6%).

Zirconium tetra-(1 : 1 : 2-*trimethylpropoxide*). Zirconium *iso*propoxide (7·4 g.) in benzene (80 c.c.) was caused to react with 1 : 1 : 2-trimethylpropanol, and the new *alkoxide* was isolated in the usual manner. On distillation a residue remained and the distillate was a brown mobile liquid (5·6 g.). Redistillation gave, with slight decomposition, a pale yellow liquid (4·5 g.), b. p. 133°/0·1 mm. (Found : Zr, 17·2; C, 61·2; H, 10·7. Calc. for $C_{24}H_{52}O_4Zr$: Zr, 18·4; C, 58·1; H, 10·1%). The zirconium alkoxide was evidently contaminated by *ca.* 5% of an organic substance from which it could not be separated by distillation. Although the experiment was repeated with a newly synthesised sample of 1 : 1 : 2-trimethylpropanol similar results were obtained and the alkoxide boiled at 150°/1·0 mm.

Titanium tetra-(1 : 1 : 2 : 2-*tetramethylpropoxide*). The interchange involving titanium *iso*propoxide (4·3 g.) and 1 : 1 : 2 : 2-tetramethylpropanol (8·2 g.; b. p. 131°/757 mm.) in benzene (80 c.c.) required 6 hours for completion. The new *alkoxide* was obtained as a pale yellow very viscous distillate (5·4 g.), b. p. 163°/0·5 mm. (Found : Ti, 9·45. $C_{28}H_{60}O_4Ti$ requires Ti, 9·4%).

Zirconium tetra-(1 : 1 : 2 : 2-*tetramethylpropoxide*). The addition of 1 : 1 : 2 : 2-tetramethylpropanol (6·1 g.) to zirconium *iso*propoxide (4·7 g.) produced an instant yellow coloration. After the addition of benzene (80 c.c.) the reaction was carried out in the usual way but was so slow that only a few drops of azeotrope were obtained and most of the distillate boiled between 76° and 77°. The new zirconium *alkoxide* was distilled (163°/0·3 mm.) with difficulty, owing to its tendency

to block the apparatus. Redistillation gave a yellow solid (b. p. 168°/0·5 mm.) (Found: Zr, 16·6; C, 58·6; H, 10·3. $C_{28}H_{60}O_4Zr$ requires Zr, 16·5; C, 60·9; H, 11·0%).

Titanium tetra-(1-ethyl-1 : 2-dimethylpropoxide). Titanium *iso*propoxide (3·0 g.) and 1-ethyl-1 : 2-dimethylpropanol (6·5 g.; b. p. 142°/765 mm.) were heated together at 150—160° in benzene (70 c.c.) for 4 hours before the interchange was complete. The new *alkoxide* was distilled (197°/1·0 mm.) and set to a very viscous colourless liquid (4·2 g.) (Found: Ti, 9·5; C, 66·3; H, 11·6. $C_{28}H_{60}O_4Ti$ requires Ti, 9·4; C, 66·1; H, 11·9%).

Zirconium tetra-(1-ethyl-1 : 2-dimethylpropoxide). The interchange involving 1-ethyl-1 : 2-dimethylpropanol (5·9 g.) and zirconium *iso*propoxide (4·0 g.) in benzene (90 c.c.) required 12 hours for completion. The new *alkoxide* was a mobile liquid (4·2 g.), b. p. 194°/0·7 mm. (Found: Zr, 16·5; C, 60·7; H, 10·8. $C_{28}H_{60}O_4Zr$ requires Zr, 16·5; C, 60·9; H, 11·0%).

Titanium tetra-(1 : 1-diethylpropoxide). From the reaction involving titanium *iso*propoxide (3·5 g.) and 1 : 1-diethylpropanol (7·5 g.; b. p. 142°/758 mm.) in benzene (80 c.c.) the new *alkoxide* was recovered in the usual way. The compound was distilled with difficulty (m. p. 140°; b. p. 180°/0·5 mm.) and the colourless distillate set to a glass (Found: Ti, 9·5; C, 66·2; H, 12·0. $C_{28}H_{60}O_4Ti$ requires Ti, 9·4; C, 66·1; H, 11·9%).

Zirconium tetra-(1 : 1-diethylpropoxide). Zirconium *iso*propoxide (8·7 g.) and 1 : 1-diethylpropanol (13·5 g.) were caused to react in benzene (80 c.c.), and the new *alkoxide* was isolated as before. The colourless product (10·3 g.) set to a glass after distillation (180°/0·4 mm.) (Found: Zr, 16·6; C, 59·7; H, 10·85. $C_{28}H_{60}O_4Zr$ requires Zr, 16·5; C, 60·9; H, 11·0%).

Reaction between Ethyl Orthosilicate and 1 : 1-Dimethylpropanol.—Ethyl orthosilicate (3·9 g.; prepared from ethanol and silicon tetrachloride) and 1 : 1-dimethylpropanol (9·1 g.) were heated together at 140—150° in benzene (60 c.c.) in the apparatus containing the fractionating column (70 cm.) Throughout 8 hours the b. p. under total reflux remained constant at that of pure benzene, showing that no interchange had occurred. On addition of zirconium tetra-1 : 1-dimethylpropoxide (1·0 g.) as a catalyst the b. p. fell to 70° in 20 minutes. Removal of distillate (6·0 c.c.; b. p. 72—73°) caused a rise in b. p. and fractionation was continued at a high reflux ratio until pure benzene was collected. After removal of solvent the liquid mixed alkoxide was distilled under atmospheric pressure and gave a main fraction boiling at 180—185° [Found: Si, 10·5; Zr, <0·2. Calc. for $Si(OEt)_3 \cdot OC_5H_{11}$: Si, 11·2%]. The residual liquid distilled at 210°/200 mm. (Found: Zr, 12·3; Si, 4·1%).

Fractional Distillation of Zirconium Tetra-(1 : 1-dimethylpropoxide).—Zirconium tetra-1 : 1-dimethylpropoxide (25 g.; containing HfO_2, 2·1% based on the mixed oxides) was fractionated at 160—180° through a column (45 cm.) packed with Fenske helices. The distillate (1 c.c.; b. p. 100°/0·3 mm.) was collected at a 10 : 1 reflux ratio (Found: Hf, 3·2 ± 0·2%). The experiment was terminated because of leakage, the remaining alkoxide containing 2·1 ± 0·2% of hafnium.

A second sample (47·5 g.; Hf, 0·8 ± 0·1%) was fractionated in the same apparatus at the reflux ratio 10 : 1. The first fraction (7·5 g.; b. p. 100°/0·3 mm.; Hf, 1·2 ± 0·1%) was again enriched in hafnium. Flooding and decomposition then interfered with fractionation and the combined second and third fractions (25 g.) had the same hafnium content (0·8 ± 0·1%) as the initial material. The remaining undistilled alkoxide had a slightly lower hafnium content (0·7 ± 0·1%). It is hoped that with an improved design of apparatus it will be possible to separate hafnium from zirconium by this method.

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810. *Some Structural Properties of* α-MnO_2 *containing* NH_4^+, K^+, Na^+, Ca^{++}, *and* Ba^{++} *Ions.*

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Methods of obtaining α-MnO_2 containing Na^+, K^+, NH_4^+, Ca^{++}, and Ba^{++} ions, either directly or by sintering manganous manganite, are described. The formation of the α-phase is shown to be accompanied by a loss in oxygen until the ratio oxygen : manganese reaches the value 1·88 characteristic of the α-form. The structures of the materials were examined by *X*-ray and electron diffraction and electron microscopy. The macroscopic crystals of the potassium- and ammonium-containing oxides are straw-shaped; the others do not show this habit. All the oxides have layers of MnO and either γ-Mn_2O_3 or Mn_3O_4 on the surface.

The designation α has been applied to varieties of naturally occurring manganese dioxide containing foreign ions and crystallising with a tetragonal, or pseudo-tetragonal (monoclinic, $\beta \simeq 90°$; $a_0 \simeq c_0$), structure with a large axial ratio. An approximate general formula for these oxides is $M_xMn_8O_{16}$, where M is the foreign metal ion and x varies, but is usually less than 2.

Much of the work on these oxides has been carried out with naturally occurring minerals and relevant details are given on p. 4213. Our interest in the systems arises out of our investigations on the synthetic production of different types of manganese dioxide. The problem has been studied to some extent by other workers; *e.g.*, Sakar and Dhar (*Z. anorg. Chem.*, 1922, **121**, 135) investigated the precipitation of manganese dioxide from manganese sulphate by potassium permanganate in the presence of foreign ions. Many of the oxides obtained had a general formula of $MO,7MnO_2$ with a high but variable water content, *e.g.*, $CaO,7MnO_2,14H_2O$. Oxides of similar composition can also be prepared by shaking freshly precipitated manganese dioxide with a solution containing the foreign ion. We have already obtained indications that M may be ammonium (Butler and Thirsk, *Acta Cryst.*, 1952, **5**, 288). Other references to the preparation of oxides having an α-MnO_2 structure are by Dubois (*Ann. Chim.*, 1936, **5**, 401), who also claimed to have prepared an α-MnO_2 containing no foreign ion by decomposing permanganic acid. It is possible that his preparation may contain some barium. These results have led us to investigate the possibility of preparing α-oxides with M = Ba, Ca, K, or Na.

We have either used a method whereby α-MnO_2 is produced directly, or have prepared samples of manganous manganite, which is known to yield the α-oxide on sintering. By manganous manganite, we mean essentially finely divided oxides giving prominent diffractions near $d_{hkl} = 7·3$, 3·6, 2·45, and 1·41 Å, and we thus use the designation due to Feitknecht and Marti (*Helv. Chim. Acta*, 1945, **28**, 129) in classifying certain preparations from *X*-ray data. We do not, however, limit ourselves, as they do, to a method of preparation by oxidation of alkaline manganese solutions.

The chemical compositions have been determined of the precipitates (i) as originally formed, after suitable methods of drying, and (ii) during the sintering processes at different temperatures. The changes in the structure of the oxides during the heating process have been examined by *X*-ray and electron diffraction. Electron microscopy has been used in an attempt to follow changes in the shape of the micro-crystals of the oxides during the sintering process, and electron diffraction in an attempt to increase the resolution of the diffraction method particularly in size ranges where *X*-rays give diffuse patterns. By using the EM3 Metropolitan-Vickers microscope, a simultaneous search of the oxide specimen by microscopy and diffraction was possible. As shown previously (Butler and Thirsk, *loc. cit.*) in certain cases, the high resolution of the instrument makes it possible to ascribe a particular orientation to the unit cell in the observed crystals.

Experimental

X-*Ray, Electron-microscope, and Election-diffraction Techniques.*—Photographs of the manganese oxides were taken on a Metropolitan-Vickers demountable *X*-ray set, a 9-cm. powder

camera being used. Unfiltered iron radiation was used, the manganese dioxide specimen acting as its own β-filter. This resulted in a somewhat darkened back-ground but only the weakest reflections are lost. The normal exposure at 44 kv and 18 mA was 90 minutes.

Rod-shaped specimens of diameter about 0·3 mm. were made by intimately mixing the oxide with gum tragacanth, moistening it with water to a very stiff paste, and rolling it between two glass slides until dry. These rods were mounted centrally in the camera in the usual way.

The line positions on the films were measured by means of an instrument designed by Gibson (*J. Sci. Instr.*, 1946, **23**, 159). The wave-length of the α-radiation of iron was taken to be 1·9373 Å. Some use was made, in addition to the EM3 instrument, of an electron-diffraction camera of the type described by Finch and Wilman (*Ergebn. exakt. Naturwiss.*, 1937, **16**, 353).

The specimens for examination in these two instruments were supported on Collodion or Formvar films picked up on the standard copper gauzes used in the electron microscope. Deposits were made either by precipitation from air (Drummond *et al.*, *J. Roy. Micros. Soc.*, 1950, **70**, 32), or by evaporation of a drop of an aqueous suspension which was placed on the film by means of a platinum ring. We could not detect any difference between the results by the two methods.

For an accurate determination of the interplanar spacings, we used thallous chloride as standard, and $a_0 = 3{\cdot}834$ Å was taken as the length of the edge of the simple cubic unit cell. This standard was suggested by Boswell (*Proc. Phys. Soc.*, 1951, *A*, **64**, 465), and we found that the material gave very sharp lines whether it was evaporated on to the oxide specimen or co-deposited from a solution containing the suspended oxide.

All the plates were measured by a travelling microscope adapted to project the image of a cross-wire on to the photographic plate.

Preparative and Analytical Techniques.—" AnalaR " reagents were used for all preparations and analyses.

Preparation 1. The procedure was similar to that used by Selwood, Eischens, Ellis, and Wethington (*J. Amer. Chem. Soc.*, 1949, **71**, 3039) for the preparation of the oxide they describe as γ(I)-MnO_2. 50 G. of hydrated manganese sulphate and 100 ml. of 2N-sulphuric acid were dissolved in 1 l. of water. The solution was then heated to boiling, and 113 g. of ammonium persulphate were added in small portions during ½ hour. The precipitate formed was washed by decantation with boiling water and finally collected and washed again with hot water. Preparation 1(*a*) was dried for 6 days at 60°, and 1(*b*) for 6 days in a vacuum-desiccator (P_2O_5).

Preparation 2. The method was similar to that used by Selwood *et al.* (*loc. cit.*) for the preparation they name γ(II)-MnO_2. A solution of hydrated manganese sulphate (36 g.) and potassium nitrate (24 g.) in water (about 2 l.) was heated to boiling, and 2% potassium permanganate solution slowly added until present in excess. The precipitate was washed by decantation with boiling water (6 × 1 l.), then filtered off and washed again. Preparations 2(*a*) and 2(*b*) were dried as for 1(*a*) and 1(*b*), respectively.

Preparation 3. 5N-Solutions were made of the permanganates of (*a*) potassium, (*b*) sodium, (*c*) calcium, and (*d*) barium. 60 ml. of each of the solutions were boiled, and 15 ml. of *ca.* 6N-hydrochloric acid (redistilled) slowly added. The precipitates were washed with boiling water and dried as for preparations (*b*), above.

Analysis. The oxides were analysed for manganese, available oxygen (*i.e.*, the excess over that required for MnO), water, and the foreign ion.

Manganese was determined volumetrically by means of the pyrophosphate complex of tervalent manganese (Goffart, Michel, and Pitance, *Anal. Chim. Acta*, 1947, **1**, No. 6, 393). To this end, the oxide was dissolved in a small amount of hydrochloric acid, and the solution made up to 300 c.c. by addition of a freshly saturated solution of sodium pyrophosphate. The pH of the solution was then adjusted to between 6 and 8 by addition of sodium hydroxide solution, litmus paper being the indicator. The resulting solution was titrated with standard potassium permanganate, the end-point being detected by a platinum and silver/silver chloride electrode connected externally to a micro-ammeter. The permanganate solution was standardised against sodium oxalate (Fowler and Bright, *J. Res. Nat. Bur. Stand.*, 1935, **15**, 497).

Available oxygen was determined by Eberius and Le Blanc's modification (*Z. physikal. Chem.*, 1932, **160**, *A*, 129) of Bunsen's method. The oxide was heated with hydrochloric acid, and the chlorine evolved carried by a stream of carbon dioxide into the absorption vessels containing potassium iodide solution. The iodine liberated was titrated with sodium thiosulphate solution which had been standardised against potassium iodate.

The combination of these two methods has the advantage that the oxygen : manganese ratio can be determined rapidly on a sample of manganese dioxide without any standardisation of

solution or weighing: the available oxygen is first determined on any weight of manganese dioxide and the remaining solution is used for determination of the manganese. Water was determined by Penfield's method (*Amer. J. Sci.*, 1894, **48**, 30) modified to accommodate the very bulky specimens by blowing a bulb on the end of the tube containing the dioxide. Potassium was determined by means of a flame photometer, barium and calcium by precipitation as sulphate, and the sodium by difference. Ammonia was determined by a modified Kjeldahl method.

Sintering Experiments.—The specimens of the oxide were sintered by heating them in a hard-glass tube which had a small furnace placed round the centre. A current of dry oxygen was passed over the specimen, and the temperature measured by means of a thermocouple. The apparatus permitted sintering to be carried out at temperatures up to about 580°. Two of the preparations, those containing calcium and barium, were also sintered at a red heat but in this case they were exposed to the air. A preliminary survey of the behaviour of the oxide on heating was carried out by differential thermal analysis. The conditions of sintering were then chosen so that, except for Preps. 3(*c*) and (*d*) at above 500°, very little decomposition of the oxide was believed to occur. Heating was for 24 hours at each temperature except where otherwise noted.

Results.—Preparation 1. Prep. 1(*a*) had a composition by analysis of $(NH_4)_{0\cdot016}MnO_{1\cdot884},0\cdot33H_2O$; and 1(*b*) of $(NH_4)_{0\cdot022}MnO_{1\cdot951},0\cdot26H_2O$. *X*-Ray data gave evidence in 1(*a*) of equal amounts of α- and γ-oxide. Previous workers had found only the γ-phase; we have also prepared the pure γ-form by using this method. The lines were broad, indicating very fine crystals. The dimensions of the unit cell of the α-form were $a_0 = 9\cdot87 \pm 0\cdot02$ Å, $c_0 = 2\cdot849 \pm 0\cdot005$ Å, $a/c = 3\cdot46$. Similarly, Prep. 1(*b*) was also a mixture of α- and γ-MnO_2. Heating to 200° gave very similar diffraction patterns, but from the increased sharpness of the 002 diffraction it seems clear that the crystallinity of the specimens was improved. No further heating was carried out on this preparation because the crystallites seemed quite well developed; examination in the electron microscope showed that they were about 1 μ long. From the electron-diffraction patterns it was calculated that the material had an α-MnO_2 structure, with unit cell of $a_0 = 9\cdot88 \pm 0\cdot03$ Å, $c_0 = 2\cdot845 \pm 0\cdot005$ Å, $a/c = 3\cdot47$. The c_0 axis of the unit cell has been shown to lie parallel to the long axis of the needle-like aggregates (Butler and Thirsk, *loc. cit.*). The surface of the oxide showed the presence of MnO and also of either γ-Mn_2O_3 or Mn_3O_4. It is impossible to distinguish between these two oxides except by chemical analysis, since the recorded *X*-ray patterns seem to be identical.

Preparation 2. Initially Prep. 2(*a*) had the constitution $K_{0\cdot093}MnO_{1\cdot911},0\cdot34H_2O$, and Prep. 2(*b*) $K_{0\cdot085}MnO_{1\cdot931},0\cdot40H_2O$; after 24 hours' heating at 200° the compositions were $K_{0\cdot092}MnO_{1\cdot941}$ and $K_{0\cdot085}MnO_{1\cdot944}$, respectively.

The preparations gave broad diffraction lines by *X*-ray analysis and indicate almost equal amounts of α- and γ-oxide. It is considered that the increase in ratio (available O_2)/Mn on sintering is due to the γ-phase which can absorb oxygen up to practically the theoretical amount; whereas (see table) the α-phase loses oxygen when heated, approaching the limiting ratio $MnO_{1\cdot88}$ as crystal growth occurs. On balance, this mixed phase absorbs a small amount of oxygen on being heated. Heating to 200° produced a slight improvement in the crystallinity. By electron diffraction the preparation gave evidence for MnO, and γ-Mn_2O_3 or Mn_3O_4. It was clear from examination of the electron-microscope pictures that the needles of α-MnO_2 observed were much more finely divided than in Preps. 1(*a*) and 1(*b*). The α-MnO_2 pattern corresponded to a body-centred tetragonal lattice with $a_0 = 9\cdot83 \pm 0\cdot01$ Å, $c_0 = 2\cdot862 \pm 0\cdot003$ Å, $a/c = 3\cdot434$. The elongation of the crystals in the direction of the c_0 axis in the unit cell was not so marked as in the first preparation.

Preparation 3. The preparation was analysed in its initial form, and after it had been heated at 200° and at 400°, the compositions were $K_{0\cdot278}MnO_{2\cdot00},0\cdot82H_2O$, $K_{0\cdot278}MnO_{1\cdot928}$, and $K_{0\cdot278}MnO_{1\cdot892}$, respectively.

Prep. 3(*a*) gave four broad refractions characteristic of manganous manganite. At 200° the crystallinity was improved, the unit-cell dimensions being $a_0 = 10\cdot3$ Å, $c_0 = 2\cdot83$ Å. At 400° manganous manganite was transformed with considerable improvement in crystallinity into α-MnO_2, with unit-cell parameters $a_0 = 9\cdot82 \pm 0\cdot01$ Å, $c_0 = 2\cdot858 \pm 0\cdot005$ Å. The improvement in crystallinity at 200° was quite noticeable by electron microscopy, but no preferred direction of growth could be observed in the crystalline aggregates. At this temperature no α-MnO_2 was detectable, although the diffraction rings for the γ-Mn_2O_3 or Mn_3O_4 were broken, indicating that the lower dioxide particles were of greater size than in the original preparation. Heating at 400° caused a marked change, and the preparation showed well-

developed needle-like crystals, giving an α-MnO_2 pattern similar to that of Preps. 1 and 2. The c_0 axis in the unit cell was again seen to lie in the direction of the long axis of the needles.

Prep. 3(*b*) was very similar to 3(*a*) and at 200° the unit-cell dimensions of the manganous manganite were as recorded for 3(*a*). The following analytical data were obtained. For the original preparation the formula was $Na_{0\cdot218}MnO_{1\cdot987}.1\cdot14H_2O$; after heating to 200°, $Na_{0\cdot218}MnO_{1\cdot932}$, and after heating to 400°, $Na_{0\cdot218}MnO_{1\cdot895}$. It was noted from *X*-ray diffraction that at 400° transformation took place into α-MnO_2, with a body-centred tetragonal unit cell: $a_0 = 9\cdot81 \pm 0\cdot02$ Å, $c_0 = 2\cdot858 \pm 0\cdot005$ Å. This preparation gave much more diffuse reflections than the α-MnO_2 from Prep. 3(*a*). On examining the specimen by electron microscopy it was noticed that the crystals, although giving α-MnO_2 diffraction patterns, had grown in quite a uniform crystal habit. No evidence was found on further examination by electron diffraction of any preferred external shape or internal structure for the α-MnO_2. The diffraction spots lying on the diffraction rings corresponding to α-MnO_2 were quite round and not elongated in specific directions.

X-Ray evidence showed that Prep. 3(*c*) was very poorly crystalline indeed. On heating to 400°, three diffuse lines were obtained. These could be indexed on a unit cell with $a_0 = 10\cdot5$ Å and $c_0 = 2\cdot82$ Å, assigned as 200, 121, and 002 reflections; manganese manganite gives 110, 220, 121, and 002 reflections. Attempts to improve the crystallinity of this oxide by sintering were unsuccessful. At 580° the oxide obtained was shown to be a mixture of α-MnO_2, with $a_0 = 9\cdot78 \pm 0\cdot02$ Å, $c_0 = 2\cdot847 \pm 0\cdot005$ Å, and cubic α-Mn_2O_3, with $a_0 = 9\cdot40$ Å. The compositions were: as prepared, $Ba_{0\cdot131}MnO_{2\cdot00}$; at 400°, $Ba_{0\cdot131}MnO_{1\cdot937}$, and at 500°, $Ba_{0\cdot131}MnO_{1\cdot910}$. Prep. 3(*d*) was also very poorly crystalline. Its chemical composition varied in a similar manner to that of 3(*c*). Initially the composition was $Ca_{0\cdot125}MnO_{1\cdot986}$, and after heating at 200° $Ca_{0\cdot125}MnO_{1\cdot937}$, and at 500°, $Ca_{0\cdot125}MnO_{1\cdot859}$. As will be noticed in the analysis slight decomposition had occurred at 500°.

On heating to 400°, no improvement in the crystallinity or additional diffraction lines were observed. At 500° α-MnO_2 was formed, and the crystallinity was slightly improved by further heating at 580°. The dimensions of the body-centred tetragonal unit cell were $a_0 = 9\cdot83 \pm 0\cdot02$ Å, $c_0 = 2\cdot847 \pm 0\cdot005$ Å. This oxide was stable for a short period at red heat. Similar comments can be made on the results from the electron microscope and diffraction examination. Both Preps. 3(*c*) and 3(*d*) gave sharp diffraction patterns after being heated at 580°. An attempt was made with Prep. 3(*d*) to produce further growth in the crystals by heating at a red heat, and evidence was obtained that the α-MnO_2 had decomposed considerably. The electron micrographs showed a beautiful effect: very sharply defined and regularly shaped rod-like crystals grew out of the crystalline matrix. It is considered that these crystals may be single crystals of either γ-Mn_2O_3 or Mn_3O_4, and the nature of the phase change is still being investigated. Some importance is attached to the observation that with these two preparations containing calcium and barium, increase in crystal size by sintering was much less than with α-MnO_2 containing sodium and potassium.

The final specimen examined was a commercial B.D.H. sample of composition $K_{0\cdot212}MnO_{1\cdot916}.1\cdot09H_2O$, which gave originally a manganous manganite pattern. After 100 hours' heating at 530°, it had crystallised as α-MnO_2 with $a_0 = 9\cdot828$ Å, $c_0 = 2\cdot862$ Å, $a/c = 3\cdot434$.

Discussion

In the following discussion we have represented our oxides as anhydrous material based on a general formula $M_xMn_8O_y$. The experimental results are summarised in the table. It is convenient to relate a discussion of the results from our synthetic materials with relevant data for naturally occurring minerals. The mineral hollandite corresponds to $Ba_xMn_8O_{16}$. Byström and Byström (*Acta Cryst.*, 1950, **3**, 146) determined the unit cell to be monoclinic, with dimensions $a_0 = 9\cdot91$ Å, $b_0 = 2\cdot872$ Å, $c_0 = 9\cdot97$ Å, and $\beta = 90\cdot6°$. From the short M–M distance in the crystals, they consider that for large ions the maximum value of x is about unity. If the foreign ion is potassium, the corresponding mineral is $K_xMn_8O_{16}$, cryptomelane, and Byström and Byström (*loc. cit.*) consider that x must be about 1. Delano (*Ind. Eng. Chem.*, 1950, **42**, 523) considers the correct formula to be $x = 2$. The unit cell was thought by Ramsdell (*Amer. Min.*, 1942, **27**, 611) to be tetragonal with $a_0 = 9\cdot82$ Å, $c_0 = 2\cdot86$ Å, but Byström and Byström give the unit-cell dimensions $a_0 = 9\cdot84$ Å, $c_0 = 2\cdot85$ Å, and consider that the maximum difference in length of a_0 and b_0

Summary of experimental results.

Method of preptn.	Treatment	Formula	Comments (cell dimensions in Å)
Prep. 1. $MnSO_4$ + $(NH_4)_2S_2O_8$	1(*a*). Dried for 6 days at 60°	$(NH_4)_{0\cdot18}Mn_8O_{15\cdot1}$	Broad lines by *X*-ray diffraction. Approx. equal amounts of α- and γ-forms. Unit cell of α-form has $a_0 = 9\cdot87 \pm 0\cdot02$, $c_0 = 2\cdot849 \pm 0\cdot005$, $a/c = 3\cdot46$
	1(*b*). Dried for 6 days over P_2O_5 in vac. desiccator	$(NH_4)_{0\cdot18}Mn_8O_{15\cdot61}$	
	1(*b*). Heated to 200° for 24 hours in oxygen	$(NH_4)_{0\cdot16}Mn_8O_{15\cdot82}$	Electron microscopy shows α-form to exist as straw-shaped particles about 1 μ in length; electron diffraction demonstrated that the c_0 axis lay parallel to the long axis of the crystals and gave the following dimensions for the unit cell: $a_0 = 9\cdot88 \pm 0\cdot03$, $c_0 = 2\cdot845 \pm 0\cdot005$, $a/c = 3\cdot47$. Also present were MnO, and γ-Mn_2O_3 or Mn_3O_4 on the surface
Prep. 2. Boiling solution of $MnSO_4$ and KNO_3 to which $KMnO_4$ was added	2(*a*). Dried for 6 days at 60°	$K_{0\cdot73}Mn_8O_{15\cdot29}$	Heating to 200° gives a slight improvement in crystallinity. Approx. equal amounts of α- and γ-oxides present. Less well-developed crystals of α-form than for Prep. 1. Unit cell: $a_0 = 9\cdot83 \pm 0\cdot01$, $c_0 = 2\cdot862 \pm 0\cdot03$, $a/c = 3\cdot434$
	2(*a*). Heated at 200° in oxygen for 24 hours	$K_{0\cdot73}Mn_8O_{15\cdot53}$	
	2(*b*). Dried for 6 days at 60°	$K_{0\cdot68}Mn_8O_{15\cdot46}$	
	2(*b*). Heated at 200° in oxygen for 24 hours	$K_{0\cdot68}Mn_8O_{15\cdot56}$	
Prep. 3(*a*). 6N-HCl added dropwise to a boiling 5N-solution of $KMnO_4$	3(*a*). Dried *in vacuo* over P_2O_5 for 6 days	$K_{2\cdot22}Mn_8O_{16\cdot00}$	Four broad manganous manganite reflections
	3(*a*). Heated at 200° in oxygen for 24 hours	$K_{2\cdot22}Mn_8O_{15\cdot42}$	Improved crystallinity: $a_0 = 10\cdot3$, $c_0 = 2\cdot83$
	3(*a*). Heated at 400° in oxygen for 24 hours	$K_{2\cdot22}Mn_8O_{15\cdot14}$	Similar shape of crystals to Preps. 1 and 2. Unit cell has: $a_0 = 9\cdot82 \pm 0\cdot07$, $c_0 = 2\cdot858 \pm 0\cdot005$
Prep. 3(*b*). 6N-HCl added dropwise to a boiling 5N-$NaMnO_4$ solution	3(*b*). Dried *in vacuo* over P_2O_5 for 6 days	$Na_{1\cdot75}Mn_8O_{15\cdot90}$	Manganous manganite
	3(*b*). Heated at 200° for 24 hrs. in oxygen	$Na_{1\cdot75}Mn_8O_{15\cdot46}$	Much as above; slightly more crystalline
	3(*b*). Heated at 400°	$Na_{1\cdot75}Mn_8O_{15\cdot20}$	α-MnO_2 with unit cell: $a_0 = 9\cdot81 \pm 0\cdot02$, $c_0 = 2\cdot858 \pm 0\cdot005$ No preferred direction of growth of crystalline material
3(*c*). 6N-HCl added to boiling 5N-$Ba(MnO_4)_2$	3(*d*). Dried *in vacuo* over P_2O_5 for 6 days	$Ba_{1\cdot05}Mn_8O_{16\cdot00}$	Very poorly crystalline manganous manganite
	3(*d*). Heated at 400° in O_2	$Ba_{1\cdot05}Mn_8O_{15\cdot50}$	Three broad lines from *X*-rays: $a_0 = 10\cdot5$, $c_0 = 2\cdot82$
	3(*d*). Heated at 500° in O_2	$Ba_{1\cdot05}Mn_8O_{15\cdot28}$	Little change in appearance. Finely divided α-form; some decomposition. A mixture of α-MnO_2 ($a_0 = 9\cdot87 \pm 0\cdot02$, $c_0 = 2\cdot845 \pm 0\cdot005$) and cubic Mn_2O_3 ($a_0 = 9\cdot404$). Sharp diffraction patterns
3(*d*). 6N-HCl added to boiling 5N-$Ca(MnO_4)_2$	3(*c*). Dried *in vacuo* over P_2O_5 for 6 days	$Ca_{1\cdot00}Mn_8O_{15\cdot90}$	
	3(*c*). Heated to 200° in O_2	$Ca_{1\cdot00}Mn_8O_{15\cdot74}$	Very poorly crystalline
	3(*c*). Heated to 400° in O_2		
	3(*c*). Heated to 500° in O_2	$Ca_{1\cdot00}Mn_8O_{14\cdot87}$	Some α-MnO_2 formed. Some decomposition to Mn_2O_3
	3(*c*). Heated to 580° in O_2		Improved crystallinity but also considerable decomposition. Unit cell of α-MnO_2 is $a_0 = 9\cdot83 + 0\cdot02$, $c_0 = 2\cdot847 \pm 0\cdot005$

allowable would be 0·02 Å and the difference of β from 90° is less than 0·3°. Recently, however, Mathieson and Wadsley (*ibid.*, 1950, **35**, 99) have reported the existence of a monoclinic cryptomelane with $a_0 = 9{\cdot}79$ Å, $b_0 = 2{\cdot}86$ Å, $c_0 = 9{\cdot}94$ Å, $\beta = 90°\ 37'$. It is readily seen that these values are very close to the hollandite parameter reported above. Although the ratio of barium content to the potassium content is 1 : 6, the barium content is higher than for many other crypotmelanes, and we consider that Mathieson and Wadsley are dealing with a material similar to the mineral hollandite rather than cryptomelane.

Prep. 1 containing ammonium has a remarkably low value of x. The ammonium ion seems to be very firmly held, since heating at 200°, whilst serving to remove water from the specimen, made no other appreciable difference in the composition. This low proportion of ammonium ion might reasonably be assumed to be due to adsorption rather than the formation of a compound if it were not for certain other features of the preparation. It was a most satisfactory method of obtaining a product at room temperature possessing the characteristic microcrystalline cryptomelane structure. Recent unpublished work by the authors has also shown that the specific resistance corresponds to that of α-MnO_2 and is of the order of 10^3 less than that of the manganous manganite preparations. Since there is no well-substantiated preparation of α-MnO_2 without a foreign ion in the lattice, we regard this preparation as analogous in form to the other preparations.

Consideration of the table shows that the potassium content varies from less than 1, the limit suggested by Byström and Byström, to a figure corresponding to Delano's formulation with $x = 2$. These results imply that the foreign ion content may vary widely, although a determination of the actual quantity in the lattice is not possible owing to the poor crystallinity of the specimens preventing the use of a more refined X-ray technique. Although there must have been considerable adsorption of potassium on the enormous surface area of manganous manganite, this can hardly account for such a high percentage of potassium. The same effect was noted with the sodium, barium, and calcium products. Of these three, the barium-containing material corresponds very closely to $x = 1$, agreeing with Byström and Byström.

From an examination of our X-ray results and from experimental results of Copeland, Griffiths, and Schertzinger (*Trans. Electrochem. Soc.*, 1947, **92**, 127), the improvement in crystallinity, which may perhaps also be associated with the entry of the foreign ion into the manganese dioxide lattice, can be shown in the case of potassium to alter the c/a ratio of the tetragonal cell, mainly because of a marked decrease in the a_0 value.

It has been suggested by Sakar and Dhar (*loc. cit.*) and by Gruner (*Amer. Min.*, 1943, **28**, 496) that the oxides under discussion resembled the zeolites, since the exchange of foreign ion can be readily carried out by washing with a solution containing a replacing ion in a manner analogous to zeolitic behaviour. This point has not been examined in this work but it would seem from our results that there would be a limit to the extent to which this process can be carried out in view of the markedly differing external crystal habits of the oxides on sintering.

We thank Professor Wynne-Jones for the facilities he has placed at our disposal, Mr. E. Boult for his assistance in the operation of the electron microscope, and Dr. Smart, of the Royal Victoria Infirmary, for placing at our disposal a flame photometer facilitating the potassium estimations.

KING'S COLLEGE, NEWCASTLE-ON-TYNE. [*Received, June 18th*, 1952.]

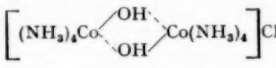
811. *A New Reagent for the Precipitation of Sulphate.*

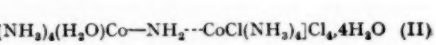
By R. Belcher and D. Gibbons.

Five co-ordination compounds of cobalt have been examined as precipitants for the sulphate ion. A gravimetric procedure has been developed using one of these compounds, *viz.*, octa-ammino-μ-amino-μ-nitro-dicobaltic nitrate. Since the precipitate is more soluble than barium sulphate, careful control of the volumes of the solution is necessary to obtain quantitative results. However, the method has the advantage that interferences are few and, in particular, the nitrate ion has no effect.

The classical method for the determination of sulphate, by precipitation as the barium salt, is subject to co-precipitation errors. In particular, the nitrate ion interferes and must be removed by evaporation with hydrochloric acid. A common alternative method of precipitation is as benzidine sulphate, but the unfavourable solubility of the precipitate, together with the disturbing effect of other ions, renders it suitable only for work where great accuracy is not required. The only other method recorded utilises precipitation as the complex hexa-amminocobaltic bromide sulphate (Mahr and Krauss, *Z. anal. Chem.*, 1948, **128**, 477) but further studies of the method are lacking.

We have examined five co-ordination compounds, which are recorded as having difficultly soluble sulphates, as possible reagents for the precipitation of sulphate, in order to find if they possessed any advantages over existing reagents. The compounds examined were octa-ammino-μ-dihydroxodicobaltic chloride, chloroaquo-octa-ammino-μ-aminodicobaltic chloride, octa-ammino-μ-amino-μ-peroxocobalt(III)–cobalt(IV) nitrate, octa-ammino-μ-amino-μ-nitrodicobaltic nitrate, octa-ammino-μ-amino-μ-hydroxodicobaltic nitrate. Of these, (IV) was the most promising, and a detailed study has been made of its use as a precipitant for sulphate. Because the sulphate is more soluble than barium sulphate, it is necessary to work in controlled volumes of solution, but co-precipitation errors appear to be negligible and the nitrate ion does not interfere.


(I)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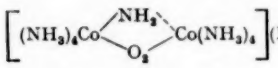
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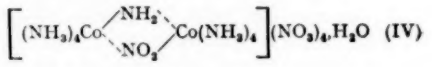
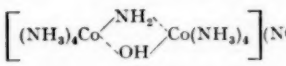

(IV)


(V)

Stability of Reagents.—(V) was very unstable, and decomposition occurred during the standing time of the precipitated sulphate. Since quantitative recovery was not possible, the compound was not examined further. (I), (II), and (III) decomposed in solution after a few hours, yielding dark precipitates; (IV) was unchanged, however, even after its solution had been kept for a week.

Sensitivity of Reagents.—Tests showed that there was little difference in sensitivity between the reagents in neutral solution. Accordingly, (I)—(IV) were subjected to further examination.

Interfering Ions.—The interfering effect of a selected number of ions was examined. The quantitative recovery of sulphate ion, illustrated by representative data in Table 3, shows that interference from the ions listed is negligible, even if they are present in 5-fold molecular proportion, when precipitation is effected under the conditions specified. The ions Na^+, K^+, Ca^{2+}, F^-, Cl^-, NO_3^-, and O_2^{2-} did not yield precipitates, even when present in a ten-fold excess. The ions Fe^{3+} and Al^{3+} interfered by hydrolysis in neutral solution, causing apparent high recoveries. When the acidity was raised sufficiently to counteract this effect, the sensitivities were greatly reduced owing to the enhanced solubility of the precipitates. Tartrate, citrate, and fluoride ions were used in an attempt to suppress the

hydrolysis, but the complexes formed interfered. However, it was found that ethylenediaminetetra-acetic acid (" enta ") (2 ml. of 0·5M-solution per millimole of Fe or Al) formed complexes with both metals satisfactorily without interfering with the precipitation. The solution could then be adjusted to neutrality.

Phosphate interfered by forming a precipitate of the corresponding phosphate unless the pH of the solution was not greater than 5. At this level, only the sensitivity of (IV) was unimpaired, the solubilities of the sulphates of (I), (II), and (III) being markedly affected. With (IV), the solubility of the sulphate was not affected even at pH 4.

Further examination was confined to (IV) because of its advantages as regards stability and the solubility of the sulphate under acid conditions.

TABLE 1. *Effect of standing time on recovery from* 20·17 *mg. of sulphate* (*as* SO_4^{2-}).

Time (hr.)	Final vol. (ml.)	Recoveries (mg.)	Time (hr.)	Final vol. (ml.)	Recoveries (mg.)
0·25	100	18·14, 17·98	24·0	50	20·08, 20·04
2·0	100	18·42, 18·68	6·0	100	20·16, 20·12 *
6·0	100	18·92, 19·08	24·0	100	20·20, 20·14 *
24·0	100	19·97, 20·01	2·0	50	20·12, 20·06 *
4·0	50	19·06, 19·12	4·0	50	20·21, 20·14 *

* The final volume contained 25% (v/v) of acetone in these eight runs.

TABLE 2. *Recoveries under different conditions of standing and concentration* (all weights in mg.).

SO_4 present	SO_4 found	SO_4 present	SO_4 found
	4 Hrs.' standing.	Final vol., 20 ml.	
1·01	0·98, 0·95	2·02	2·01, 1·98
5·09	4·98, 5·04	10·19	10·15, 10·19
15·12	15·14, 15·07		
	4 Hrs.' standing.	Final vol., 50 ml.	
10·19	10·14, 10·19	15·12	15·16, 15·08
20·17	20·21, 20·14	35·29	35·32, 35·27
50·43	50·45, 50·42		
	½ Hrs.' standing.	Final vol., 50 ml.	
50·43	50·41, 50·46	60·51	60·53, 60·47
80·68	80·66, 80·72	100·85	100·81, 100·89

TABLE 3. *Effect of other ions on recoveries from* 20·17 *mg. of sulphate* (*as* SO_4^{2-})

Ion	Recoveries (mg.) *	Ion	Recoveries (mg.) *	Ion	Recoveries (mg.) *
Na^+	20·16, 20·16	Fe^{3+} (enta)	20·22, 20·21	O_2^{2+}	20·16, 20·15 †
K^+	20·15, 20·17	Cl^-	20·20, 20·19	H^+	20·18, 20·14 ‡
Ca^{2+}	20·23, 20·20	F^-	20·21, 20·20	$(H^+) + PO_4^{3-}$	20·16, 20·19
Al^{3+} (enta)	20·19, 20·20	NO_3^-	20·16, 20·16		

* In each pair, the first relates to the presence of 1 ml., and the second to that of 5 ml., of an M/5-solution of the ion concerned, except in the three cases specially noted.
† Recoveries were in presence of 1 and 5 ml., respectively, of 100-vol. H_2O_2.
‡ Second entry relates to only 2 ml. of M/5-H^+.

Solubility of Sulphate of (IV).—The solubility in water at 25° was found to be 22·4 mg. per l.; this compares unfavourably with that of barium sulphate (2·3 mg./l. at 18°), but it is much better than that of benzidine sulphate (98 mg./l. at 25°). However, the solubility figures in water can only serve as a rough guide, since the precipitate may be more or less soluble in the presence of excess of reagent and under the conditions of precipitation.

Recoveries under Various Conditions in using (IV).—The effects of standing time and volume of solution were examined, the results being included in Tables 1 and 2. It was found that the precipitate could either be dried at 110° or washed with acetone and air-dried. The presence of acetone effected a more marked improvement of the recoveries than that of ethanol or methanol. These results were taken into account in devising the recommended procedure (p. 4218).

The method might be of particular use in the determination of sulphur in organic

compounds containing nitrogen, by combustion on the micro-scale. In this procedure it is necessary to eliminate the nitric acid formed before precipitation of sulphate as barium sulphate. Since hydrogen peroxide, which is normally used as the absorbent for products of combustion, does not interfere, it would not be necessary to eliminate it first.

Experimental

Preparation of Reagents.—(I) and (III) were prepared by Werner's methods (*Ber.*, 1907, **40**, 4437, 4609); (II) by that of Werner and Salzer (*Annalen*, 1910, **375**, 45); (V) by that of Werner and Baselli (*Z. anorg. Chem.*, 1898, **16**, 150); and (IV) by that of Werner, Salzer, and Pieper (*Annalen*, 1910, **375**, 54).

Determination of Solubility of Sulphate of (IV).—About 50 mg. of the sulphate were vigorously stirred with 200 ml. of water in a 250-ml. conical flask in a thermostat kept at 25° ± 0·1°. After 3 days, 100 ml. of the solution were withdrawn through a filter-stick and evaporated to dryness in a platinium dish on a steam-bath. The heating was then continued to constant weight. A blank experiment was carried out on the water used.

Recoveries.—A sulphate solution (~2 g./l.) was prepared from " AnalaR " sodium sulphate and standardised gravimetrically. A freshly prepared solution of a known excess of the reagent, in a suitable solvent, was added to a measured volume of the sulphate solution, and the mixture was well stirred and set aside. After a given time, the precipitate was filtered off on a No. 4 sintered-glass crucible, and dried by one of two methods: (*a*) after being washed with the solvent used, it was heated at 100—110° to constant weight (an hour was ample), allowed to cool in an empty desiccator, and weighed; (*b*) after being washed with the solvent used and then with acetone, the precipitate was dried in a current of air for 15 minutes, a dust-filter being used, and then weighed as before.

Recommended Procedures.—(*a*) 1—15 *Mg. of sulphate* (*as* $SO_4^{=}$). The solution was evaporated to a small enough bulk to give a final volume of 20 ml. after addition of all reagents. Sufficient " enta " (2 ml. of a 0·5M-solution per mg.-atom of Fe or Al) was added to complex any iron or aluminium present, and the solution adjusted to neutrality. If phosphate was present, 1 ml. of M/5-hydrochloric acid was added. Sufficient of a 1% solution of (IV) was added to give a 2—3 fold excess (*i.e.*, 0·3 ml./mg. of sulphate), acetone was added to give a concentration of 25% (v/v), and the mixture was kept for 4 hours with occasional stirring. The precipitate was filtered off on a No. 4 sintered-glass crucible, washed with 25% acetone and then with acetone, and then dried in a current of air (dust-filter). The crucible was kept for 30 minutes in the balance case before being weighed. Air-drying was preferred as it was quicker and less troublesome than oven-drying. The respective factors for conversion into SO_4 are: air-drying, 0·353 ($2H_2O$ of crystallisation); oven-drying, 0·378 (anhydrous).

(*b*) 15—20 *Mg. of sulphate* (*as* $SO_4^{=}$). The procedure was as above, but a final volume of 50 ml. could be used.

(*c*) 50—100 *Mg. of sulphate* (*as* $SO_4^{=}$). The procedure was as in (*b*), but the precipitate was filtered off after 30 minutes' standing.

One of us (D. G.) is indebted to the Department of Scientific and Industrial Research for a grant enabling him to carry out this work.

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[*Received, July 26th*, 1952.]

812. *Pteridine Studies. Part III.* The Solubility and the Stability to Hydrolysis of Pteridines.*

By Adrien Albert, D. J. Brown, and Gordon Cheeseman.

Two important correlations between structure and properties in the pteridine series are reported and discussed.

The introduction of OH, NH_2, and SH groups into pteridine (I) (which is highly soluble in water, hydrocarbons, and other organic solvents) greatly lowers the solubility in all solvents. Evidence is brought forward that this effect is due to unusually strong crystal-lattice forces operating through hydrogen-bonding.

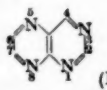
The insertion of one or (better) two electron-releasing groups into pteridine (which is readily decomposed by cold acids and alkalis) has a strong stabilizing effect. The instability of pteridine is attributed to loss of aromatic character caused by the high N : C ratio; the restoration of typical aromatic stability by OH and NH_2 groups is attributed to their ability to supply electrons to the depleted orbitals. As a practical application of this correlation, it is shown that 2-aminopyrazine-3-carboxylic acid and its derivatives can be prepared (by alkaline hydrolysis) from 4-hydroxypteridines under milder conditions than from the commonly used 2 : 4-dihydroxypteridines.

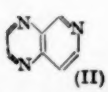
Syntheses of 2- and 4-methoxy-, 2-methylamino-, 4-dimethylamino-, 4-chloro-pteridine, 4-hydroxy-6- and -7-methylpteridine, and several 6 : 7-diethyl derivatives of hydroxy- and amino-pteridines are reported.

Ultra-violet spectra and ionization constants have been measured and correlated with structure.

Solubilities.—Insufficient attention has been paid to the decreased solubility conferred upon nitrogenous heteroaromatic substances by the insertion of amino-, hydroxy-, and thiol groups. These groups almost invariably increase the solubility in water of aliphatic and aromatic substances. For example, *m*-phenylenediamine is soluble in 1 part of water, whereas aniline and benzene (although both are liquids with no crystal-lattice forces to overcome) require 37 and 660 parts respectively. Again, 1 : 2 : 3-trihydroxybenzene requires 2 parts, 1 : 2-dihydroxybenzene 3 parts, and phenol 14 parts (all solubilities reported in this paper are for 20° unless otherwise specified).

That these groups can act in the opposite way upon heterocyclic substances was first demonstrated quantitatively in the acridine series, *e.g.*, all five monoaminoacridines are 2—5 times less soluble than acridine (Albert, " The Acridines," London, Edward Arnold and Co., 1951, pp. 152, 157). The hydroxyacridines are also less soluble than acridine. This insolubilizing effect increases as the number of amino- or hydroxy-groups is increased (4-hydroxypyridine, 1 : 1; 2 : 4-dihydroxypyridine, 1 : 160†). It also increases as the number of ring-nitrogen atoms is increased (*e.g.*, 2- and 4-hydroxy- and 2 : 4- and 4 : 6-dihydroxy-pyrimidines, 1 : 2·2,† 2·7,† 300,† and 400† respectively). This somewhat paradoxical insolubilizing effect of water-attracting groups operates even more strongly in the purine and the pteridine (I) series. The latter will now be discussed in detail.


(I)


(II)

(III)

Reference to the list of solubilities † in Table 1 shows that pteridine (No. 1) is highly soluble in water. The effect of one amino-group is to decrease the solubility 200-fold (Nos. 14—16) and of two amino-groups twice as much (No. 23). These, and the following comparisons, are made at 20° (the very high solubility of pteridine at 100° makes comparison more difficult at that temperature although the same trends are evident).

* Part II, *J.*, 1952, 1620. † New data.

The effect of one hydroxy-group is to decrease the solubility by a figure varying from 28- to 500-fold (Nos. 17—20). The effect of two hydroxy-groups is greater, varying from 100- to 700-fold (Nos. 24—27). The effect of hydroxy- is more dependent upon position than that of amino-groups, and a possible explanation will be discussed in the section on spectra, below. There appears to be a sharp rise in insolubility with three hydroxy-groups

TABLE 1. *Solubilities and melting points.*

No.	Pteridine derivative	Solubility in water 20° (±2°) 1 in	100° 1 in	M. p.	Source
1	(Unsubstituted)	7·2 †	1 ‡	140°	A
2	2-Dimethylamino	2·5 †	—	125	A
3	4-Dimethylamino	60	4	165	C
4	6-Dimethylamino *	?	—	212	B
5	2-Methoxy	80	4	150	C
6	4-Methoxy	80	9	195	C
7	6-Methoxy *	85	4	124	B
8	2-Chloro *	30	—	(dec. 106)	A
9	4-Chloro *	?	—	(dec. *ca.* 140)	C
10	6-Chloro *	80	—	(dec. 146)	B
11	3 : 4-Dihydro-4-keto-3-methyl	70	9	286	C
12	7 : 8-Dihydro-7-keto-8-methyl	50	10	125	B
13	2-Methylamino	320	35	219—220	C
14	2-Amino	1,350	100	(dec. 275)	A
15	4-Amino	1,400	80	(dec. 305)	A
16	6-Amino	1,500	110	(dec. 300)	B
17	2-Hydroxy (+1H_2O)	600	50	(dec. 240)	A
18	4-Hydroxy	200	29	>350	A
19	6-Hydroxy (+1H_2O)	3,500	230	(dec. 240)	B
20	7-Hydroxy	900	76	(dec. 230)	B
21	2-Mercapto (+1H_2O)	2,600	420	(dec. 210)	E
22	4-Mercapto	2,700	800	(dec. 290)	A
23	2 : 4-Diamino	3,000	130	(dec. 315)	C
24	2 : 4-Dihydroxy	800	120	(dec. 335)	A
25	4 : 6-Dihydroxy (+1H_2O)	5,000	300	(dec. 320)	D
26	4 : 7-Dihydroxy	4,000	600	>350	D
27	6 : 7-Dihydroxy	3,000	290	>350	B
28	4 : 6 : 7-Trihydroxy	27,000 †	7000	>350	D
29	2 : 4 : 6 : 7-Tetrahydroxy	58,000 †	—	>350	F
30	2-Amino-4-hydroxy	57,000 †	—	>350	G
31	4-Amino-2-hydroxy	14,000 †	1200	>350	C
32	2-Amino-4 : 6-dihydroxy (xanthopterin)	40,000 †	—	>350	H
33	2-Amino-4 : 6 : 7-trihydroxy (leucopterin)	750,000 †	—	>350	I
One alkyl substituent.					
34	4-Hydroxy-6-methyl	275	45	(dec. 345)	C
35	4-Hydroxy-7-methyl	225	35	(dec. >340)	C
36	4 : 7-Dihydroxy-6-methyl (+1H_2O)	800	65	>350	D
Two alkyl substituents.					
37	4-Hydroxy-6 : 7-dimethyl	1,100	100	>350	A
38	6 : 7-Diethyl	7	—	52	C
39	2-Amino-6 : 7-diethyl	5,400	—	(dec. 230)	C
40	4-Amino-6 : 7-diethyl	4,200	—	(dec. 240)	C
41	2-Hydroxy-6 : 7-diethyl (+1H_2O)	900	—	(dec. 230)	C
42	4-Hydroxy-6 : 7-diethyl	400	—	(dec. 245)	C
43	2 : 4-Diamino-6 : 7-diethyl	8,500	—	268	J
44	2 : 4-Dihydroxy-6 : 7-diethyl	1,100	—	217—219	C
45	2-Amino-4-hydroxy-6 : 7-diethyl	86,000 †	—	>350	C
46	4-Amino-2-hydroxy-6 : 7-diethyl	16,000 †	—	(dec. 290)	C
47	4-Hydroxy-6 : 7-diphenyl	5,000	—	295	C

* Substance hydrolysed by water, hence figure is only approximate. 6-Dimethylaminopteridine and 4-chloropteridine are hydrolysed too rapidly for measurement.

† Determined spectroscopically.

‡ 1 g. of pteridine is dissolved by less than 0·2 ml. of water at 100°.

Sources : A, Albert, Brown, and Cheeseman, *J.*, 1951, 474. B, *idem*, *J.*, 1952, 1620. C, Present paper. D, Forthcoming publication. E, Elion and Hitchings, *J. Amer. Chem. Soc.*, 1947, **69**, 2553. F, Bertho and Bentler, *Annalen*, 1950, **570**, 127. G, Cain, Mallette, and Taylor, *J. Amer. Chem. Soc.*, 1946, **68**, 1996; recrystallized from water instead of formic acid. H, Elion, Light, and Hitchings, *ibid.*, 1949, **71**, 741. I, Totter, *J. Biol. Chem.*, 1944, **154**, 105. J, Kindly presented by Dr. N. R. Campbell (cf. Campbell, Dunsmuir, and Fitzgerald, *J.*, 1950, 2743).

(No. 28 is 3750-fold less soluble than pteridine). Finally, tetrahydroxypteridine (No. 29) is 8500 times less soluble than pteridine. The effect of thiol (Nos. 21—22) is even greater than that of amino- or hydroxy-groups in similar positions.

The presence of both an amino- and a hydroxy-group in the one molecule decreases solubility to a greater extent than in the corresponding homogeneously substituted molecules (compare Nos. 30 and 31 with 23 or 24; 33 with 29). Leucopterin (No. 33) is of extra interest in that the addition of four water-attracting groups to pteridine has had the effect of making it more than 100,000 times less soluble.

To explain these results the hypothesis is now advanced that crystal-lattice forces, of a strength uncommonly high for organic substances, are brought into play by hydrogen-bonding between the amino-, hydroxy-, and thiol groups on the one hand and the nitrogen atoms of the pteridine ring on the other. Thus, these very hydrophilic groups exert even more attraction for one another than they do for the molecules of water.

The weightiest evidence in support of this hypothesis comes from a study of *O*-methyl-, *N*-methyl-, and chloro-pteridines. These substituents, which are not capable of hydrogen-bonding, exert a comparatively small effect on solubility [compare the dimethylamino-pteridines (Nos. 2, 3) with the aminopteridines (14—16), or the methoxypteridines (Nos. 5—7) with the hydroxypteridines (17—20)]. Likewise, the ethylthiopteridines are much more soluble than the mercaptopteridines (Polonovski, Vieillefosse, and Pesson, *Bull. Soc. chim.*, 1945, **12**, 78). Even a water-repelling substituent like chlorine does not lower the solubility more than 10-fold (Nos. 8, 10). That the diminished solubility of hydroxypteridines does not depend greatly on their being in a special configuration (*i.e.*, keto as opposed to enol) is shown by the fact that examples of both configurations, stabilized by methylation, are highly soluble (contrast No. 11 with 18, No. 12 with 20, but note the similar solubilities of Nos. 11 and 6). Thus low solubility depends much more on the presence of a bondable hydrogen atom than on a particular tautomeric configuration.

Supporting evidence is that those pteridines which have hydrogen-bonding groups (NH_2, OH, SH) show a much reduced solubility in hydrocarbon solvents (cf. Boon, Jones, and Ramage, *J.*, 1951, 96). Pteridine and the chloro-, methoxy-, and dimethylamino-pteridines dissolve in 40 parts or less of boiling benzene and can suitably be recrystallized from light petroleum, but hydrocarbon solvents do not dissolve any demonstrable amount of the amino-, hydroxy-, or mercapto-pteridines. This lack of solubility in hydrocarbon solvents indicates that the hydrogen-bonding pteridines are very highly associated.

A tendency for pteridines with hydrogen-bonding substituents to have higher melting points can be seen in Table 1, which is what would be expected where crystal-lattice forces are abnormally strong. In this connexion, it is interesting to compare pteridine (No. 1; m. p. 140°) first with the dimethylamino- and methoxy-pteridines (Nos. 2—7), which melt between 124° and 212°, and then with those pteridines having one or more hydrogen-bonding groups (Nos. 18, 27—33) which remain unmelted at 350°. A difficulty in making these comparisons arises from the fact that the majority of pteridines with only one electron-releasing group (hydroxyl, etc.) are moderately unstable (for reasons given below) and tend to decompose before the melting point is reached.

It is noteworthy that a secondary amine, 2-methylaminopteridine (No. 13), stands intermediate in solubility and melting point between the corresponding tertiary and primary amines (Nos. 2 and 14, respectively).

Normally, alkyl groups decrease the solubility of pteridines, as can be seen by comparing No. 18 with Nos. 34, 35, 37, 42, 47; No. 17 with 41; No. 14 with 39; No. 15 with 40; No. 23 with 43; No. 24 with 44; No. 30 with 45; No. 31 with 46. A striking exception is 4 : 7-dihydroxy-6-methylpteridine (No. 36) which is more soluble than 4 : 7-dihydroxypteridine (No. 26), apparently because the 6-methyl group interferes sterically with the hydrogen-bonding by the neighbouring 7-hydroxy-group.

Alkyl groups tend to lower melting points (cf. Nos. 43 and 23; 44 and 24), an effect which increases with increasing paraffin chain length until the alkyl groups, rather than the hydrogen bonds, dictate the type of crystal lattice formed. Thus, as the series of 6 : 7-dialkyl-2 : 4-diaminopteridines is ascended, the melting point falls steadily to 132° at the di-*n*-heptyl member (Campbell, Dunsmuir, and Fitzgerald, *J.*, 1950, 2743).

Stability to Alkalis and Acids.—It is commonly believed that a high degree of chemical stability is characteristic of the pteridine series. This misconception arises from the remarkable stability of many naturally occurring pteridines. For example, xanthopterin (2-amino-4 : 6-dihydroxypteridine) is unaffected by boiling 7N-hydrochloric acid and almost unaffected by boiling 1·5N-barium hydroxide during 20 hours (Wieland and Schöpf, *Ber.*, 1925, **58**, 2178; Wieland and Purrmann, *Annalen*, 1940, **544**, 163). Leucopterin (2-amino-4 : 6 : 7-trihydroxypteridine) is practically unaffected by hot concentrated sulphuric acid during 2 hours at 150° (Wieland, Metzger, Schöpf, and Bülow, *Annalen*, 1933, **507**, 226).

However, pteridine itself is a highly unstable substance, rapidly attacked by dilute acids and alkalis, even at room temperature. The monoamino- and monohydroxy-pteridines are more stable, but only substances with two such electron-releasing groups can withstand a few minutes' boiling with N-sulphuric acid or N-sodium hydroxide. The results given in Table 2 were obtained by refluxing the pteridines with acid or alkali as described in the Experimental section. The ammonia set free was determined by titration and the percentage of material not decomposed was estimated by ultra-violet spectrophotometry, all the significant peaks of all the known ionic species of each substance being used, after adjustment to the appropriate pH values. (Tri- and tetra-hydroxypteridines, which do not lend themselves to separation into ionic species, were compared with the polyanionic spectra in 0·1N-sodium hydroxide.) Each spectroscopically determined decomposition figure recorded in Table 2 was calculated from the peak showing the greatest loss in density

TABLE 2. *The percentage decomposition of pteridines.*

(After 1 hour at 110°.) (A) From ammonia evolved; (B) from spectrophotometric estimation of unchanged material.

Pteridine derivative	N-H_2SO_4 (A)	N-H_2SO_4 (B)	N-NaOH (A)	N-NaOH (B)	10N-NaOH (A)	10N-NaOH (B)
(Unsubstituted)	*	74	57	53	‡	‡
2-Hydroxy-	5	55	7	7	5	89
4-Hydroxy-	*	60	73	57	94	80
6-Hydroxy-	<5	2	0	94	3	100
7-Hydroxy-	<9	52	15	31	50	76
2 : 4-Dihydroxy-	5	6	—	—	4	4
6 : 7-Dihydroxy-	5	7	—	—	4	12
4 : 6 : 7-Trihydroxy-	†	†	—	—	1	4
2 : 4 : 6 : 7-Tetrahydroxy-	†	†	—	—	6	6

* No figure can be quoted, because much ammonia is liberated by alkaline decomposition during steam-distillation.

† Apparently unaffected; however, the very sparing solubility of these substances in boiling N-sulphuric acid prevents a just comparison with the other substance.

‡ The formation of a large quantity of tar early in this reaction produced a non-homogeneous mass.

(compared with the corresponding peak in the corresponding species of untreated substance). Thus, 6 : 7-dihydroxypteridine, after alkaline decomposition, was examined at 249 and 301 mμ (as the neutral molecule at pH 4·00), at 268, 319, and 334 mμ (as the monoanion at pH 8·40), and at 240, 324, and 338 mμ (as the dianion at pH 11·95). The percentage not decomposed appeared to be 89·9, 89·6, 100, 88·5, 87·7, 91·0, 89·8, and 90·4% respectively. Because the lowest of these figures is 87·7, the decomposition is given as 12% in Table 2. This examination of a number of peaks, and species, was designed to minimize error due to the possibility of the decomposition product(s) having some peaks at wave-lengths neighbouring on those of the starting material. A comparison of the results obtained by the two methods in Table 2 indicates that only in the case of 4-hydroxypteridine is more than one molecule of ammonia evolved per molecule of pteridine: on the other hand profound decomposition is seen in several cases without loss of nitrogen.

To explain the results in Table 2, the hypothesis is advanced that the instability of pteridine is due to the electron-attracting character of the four ring-nitrogen atoms. This leads to partial localization, on the nitrogens, of the ten π-electrons originating from the six carbon and four nitrogen atoms. Thus the aromatic stabilization to be expected from the presence of these π-electrons is much diminished (the possibility must even be enter-

tained that pteridine is, in consequence, non-planar). Substitution of the pteridine nucleus by electron-releasing groups apparently restores this deficit of electrons and thus permits normal aromatic stabilization. However, at least two such groups are necessary (Table 2) and their efficacy varies somewhat with the positions at which they are inserted.

In support of this hypothesis, the stability of other nuclei will be reviewed. Quinoline (with a N : C ratio of 1 : 9) is resistant to concentrated acid and alkali : it can be distilled over calcium oxide (Koenigs, *Ber.*, 1879, **12**, 97) and has been obtained (from aniline) in 90% yield in the presence of concentrated sulphuric acid at about 200° (Clarke and Davis, *Org. Synth.*, 1922, **2**, 79). *iso*Quinoline can be taken to dryness with 50% hydrobromic acid without decomposition (Bergstrom and Rodda, *J. Amer. Chem. Soc.*, 1940, **62**, 3030). Quinazoline (with a N : C ratio of 2 : 8) is more unstable, being slightly decomposed after evaporation at 100° with 10N-hydrochloric acid (Gabriel, *Ber.*, 1903, **36**, 800). No information is available for quinoxaline, but 2-methylquinoxaline behaves like quinazoline with hydrochloric acid (Böttcher, *Ber.*, 1913, **46**, 3085). Pyridino(3′ : 4′-2 : 3)pyrazine (II) (with a N : C ratio of 3 : 7) is described as rather unstable, particularly towards dilute acids (Koenigs, Bueren, and Jung, *Ber.*, 1936, **69**, 2690). Thus the high degree of instability shown by pteridine (N : C ratio of 4 : 6) seems to be a natural extrapolation of this sequence.

If this hypothesis is correct, other 6-membered heterocyclic rings with high N : C ratios should also be unstable unless substituted with strongly electron-releasing groups. 1 : 3 : 5-Triazine (III) is such a structure, and it is noteworthy that no attempt to prepare it has yet been successful. 2 : 4 : 6-Trimethyl-1 : 3 : 5-triazine, which should be somewhat stabilized by the three methyl groups, is completely hydrolysed to ammonia by 2N-hydrochloric acid at 20° (Grundmann and Weisse, *Ber.*, 1951, **84**, 684). This behaviour stands in marked contrast to the stability of pyridine, pyrimidine, pyrazine, and their methyl derivatives. As would be expected, the corresponding trihydroxy-derivative of triazine (cyanuric acid) is extraordinarily stable : it resists N-potassium hydroxide at 100° and survives boiling with concentrated sulphuric acid (Fischer, *Ber.*, 1898, **31**, 3273; Chevallier and Lassaigne, *Ann. Chim.*, 1820, [ii], **13**, 160).

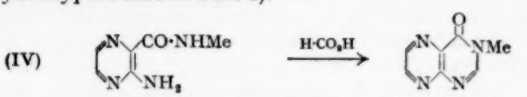
Amino-groups contribute to the stabilization of the pteridine nucleus to about the same degree as do hydroxy-groups. Furthermore the hydrolysis of amino- (and dimethylamino-) to hydroxy-compounds is itself repressed by the simultaneous presence of hydroxy-groups (see the examples of xanthopterin and leucopterin above, which stand in contrast to the easy deamination of monoaminopteridines). The stabilizing effect of amino- and hydroxy-groups is reflected in the resistance to thermal decomposition of substances containing 3 and 4 such groups (Table 1).

A small stabilizing effect from groups less powerfully electron-releasing than amino and hydroxy has been noticed. Thus 4-hydroxy-6- and -7-methylpteridine (Nos. 34, 35) require a slightly higher temperature (see below) for alkaline hydrolysis than does 4-hydroxypteridine (No. 18). 2-Amino-6 : 7-diethyl- and its 2-hydroxy-analogue (Nos. 39, 41) are not rapidly destroyed by cold 10N-hydrochloric acid or by boiling N-sodium hydroxide, but 2-amino- and 2-hydroxy-pteridine (Nos. 14, 17) are.

The outstanding stability of 6-hydroxypteridine to acid hydrolysis (Table 2) may indicate its conversion into a stable tautomer. It is noteworthy that this, alone of the monohydroxypteridines, shows hysteresis during titration (see Part II). 4-Hydroxypteridine and N-sulphuric acid gave 2-aminopyrazine-3-carboxyamide and the corresponding acid in a ratio of 1 : 2. 10N-Sodium hydroxide (at 110°) gave only 2-aminopyrazine-3-carboxylic acid. This acid is commonly prepared by heating 2 : 4-dihydroxypteridine with sodium hydroxide at 170° under pressure for 2 hours because the yield is trivial at 105° (Weijlard, Tishler, and Erickson, *J. Amer. Chem. Soc.*, 1945, **67**, 802). Thus the stabilizing effect of the extra hydroxy-group is evident. 4-Hydroxy-6- and -7-methylpteridine (see below) were also readily hydrolysed by boiling 10N-sodium hydroxide (140°) to 2-amino-6- and -5-methylpyrazine-3-carboxylic acids, which, being known substances with definite melting points, enabled the positions of the methyl groups in these pteridines to be determined.

Preparation of Pteridines.—3 : 4-Dihydro-4-keto-3-methylpteridine (V) was prepared by

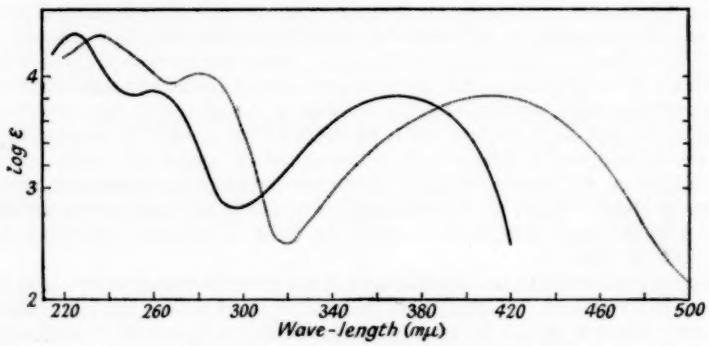
the action of formic acid on 2-aminopyrazine-3-carboxymethylamide (IV) (cf. the similar synthesis of 4-hydroxypteridine in Part I).



2- and 4-Methoxy-, 2-methylamino-, and 4-dimethylamino-pteridine were prepared by reaction of the appropriately substituted 5 : 6-diaminopyrimidines with solid polyglyoxal. Syrupy glyoxal in a neutral buffered solution was preferable for 4-chloropteridine which is more readily hydrolysed than its 2- and 6-isomers (described in Parts I and II). These conditions, applied to the synthesis of pteridine, at pH 6·5, 7·0, 7·5, and 8·0 gave a maximal yield (55%) at pH 7·0. When the synthesis of 4-chloropteridine was attempted in unbuffered methanol, a halogen-free substance was obtained, apparently glyoxylidenebis-(5-amino-4-hydroxy-6-methoxy-2-pyrimidine).

2-, 4-, and 6-Methoxypteridine were completely hydrolysed to hydroxypteridines by N-sodium hydroxide in 2 hours at 20°, or in 1 minute at the boiling point (with further

FIG. 1.



Absorption spectra in water of neutral molecules of :
——— 2-*Aminopteridine* (pH 7·1).
. . . . . 2-*Dimethylaminopteridine* (pH 7·1).

decomposition). The substance obtained in Part I by the action of perphthalic acid on pteridine in chloroform (provisionally described as pteridine *N*-oxide) has now been identified as 4-hydroxypteridine.

Methylglyoxal and 4 : 5-diamino-6-hydroxypyrimidine gave 4-hydroxy-7-methylpteridine when condensed in the presence of sodium sulphite, and 4-hydroxy-6-methylpteridine when sodium hydrogen sulphite was also present; neither product could be isolated from a reaction carried out in the absence of both these salts. The two isomers were oriented by degradation to known pyrazines.

Hexane-3 : 4-dione condensed with 4 : 5-diaminopyrimidine to give 6 : 7-diethylpteridine which has a far lower melting point (52°) than has yet been recorded for a pteridine. The dione also condensed with the appropriately substituted 4 : 5-diaminopyrimidines to give 2-(and 4-)amino-, 2-(and 4-)hydroxy-, 2 : 4-dihydroxy-, 2-amino-4-hydroxy-, and 4-amino-2-hydroxy-6 : 7-diethylpteridine. Benzil similarly gave 4-hydroxy-6 : 7-diphenylpteridine.

Spectra.—Sufficient monosubstituted pteridines are now known for preliminary investigation of tautomerism by ultra-violet spectra. The spectrum of the neutral molecule of 2-dimethylaminopteridine resembles that of 2-aminopteridine but occurs at longer wavelengths (Fig. 1). This is also true for the pair of 4- (Fig. 2) and 6-isomers (Fig. 5 of Part II), and is analogous to the shift dimethylaniline → aniline (Heertjes, Bakker, and van Kerkhof, *Rec. Trav. chim.*, 1943, **62**, 737). These results do not support an " imino "-configuration for the aminopteridines; further, recent *X*-ray crystallographic work has demonstrated the

primary character of the amino-group in 2-amino-4-methyl-6-chloropyrimidine (Clews and Cochran, *Acta Cryst.*, 1948, **1**, 4), 6-aminopurine (Broomhead, *ibid.*, p. 324), and 2 : 4 : 6-triamino-1 : 3 : 5-triazine (Hughes, *J. Amer. Chem. Soc.*, 1941, **63**, 1737; Knaggs and Lonsdale, *Proc. Roy. Soc.*, 1940, *A*, **177**, 140). Moreover, the primary character of 2-, 3-, and 4-aminopyridines has been demonstrated by infra-red spectroscopy (Goulden, *J.*, 1952, 2939).

It has been shown (Part II) that the spectrum of 7-hydroxypteridine resembles that of 7 : 8-dihydro-7-keto-8-methylpteridine (8-methyl-7-pteridone) (7-methoxypteridine is not known). The spectrum of 4-hydroxypteridine resembles those of both 3 : 4-dihydro-4-keto-3-methylpteridine (3-methyl-4-pteridone) and 4-methoxypteridine (Fig. 4). However, Figs. 3 and 5 show that the spectra of 2- and 6-hydroxypteridines do not resemble those of their methoxy-analogues (aromatic hydroxy- and methoxy-compounds usually have almost coincident spectra; Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127). Thus 2- and 6-hydroxypteridines almost certainly have the pteridone structure; there is still insufficient evidence to indicate the structure of the other two isomers. The unequal insolubilizing effect of hydroxy-groups (in contrast to amino-groups) in various positions in the pteridine ring (see Table 1) may be based, to some extent, on an unequal tendency to favour the " keto "-form : another factor may be hydrogen-bonding in solution between the 4-hydroxy-group and $N_{(5)}$.

The high degree of coincidence between the spectra of 4-aminopteridine (neutral molecule) and 4-hydroxypteridine (anion) is shown in Fig. 2. Similar pairs of curves were obtained for the 2-isomers (Part I) and the 6-isomers (Part II) (7-aminopteridine is unknown). Such relations are normal in aromatic compounds (Jones, *loc. cit.*) and suggest that the anions of 2-, 4-, and 6-hydroxypteridines are fairly normal too.

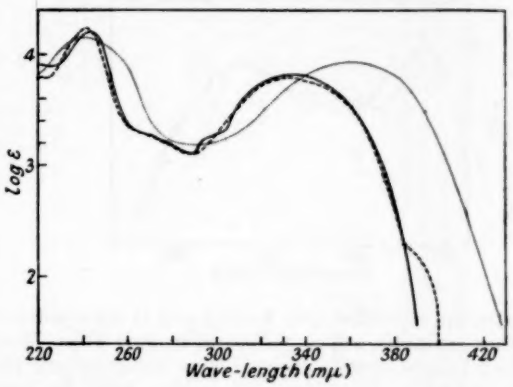


FIG. 2. *Absorption spectra in water of:*

——— 4-*Aminopteridine* (*neutral molecule*, pH 7·3).
. . . . . 4-*Dimethylaminopteridine* (*neutral molecule*, pH 7·1).
– – – – – – 4-*Hydroxypteridine* (*anion*, pH 10·0).

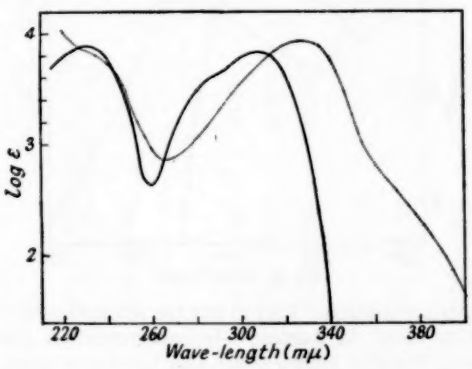


FIG. 3. *Absorption spectra in water of neutral molecules of:*

——— 2-*Hydroxypteridine* (pH 7·1).
. . . . . 2-*Methoxypteridine* (pH 6·4).

Other spectra, together with R_F and pH values, are given in Table 3 and should prove useful for identification. The spectra of the chloropteridines (see Part II, for 6-chloropteridine) closely resemble that of pteridine. An unexpected peak in 2-chloropteridine at 378 mμ led to a re-examination of the spectrum of pteridine (Part I) in *cyclo*hexane: an area of low intensity centred about 381 mμ (log ε = 1·93) was found.

Some anomalies in the spectra and ionization of amino-hydroxypteridines will now be discussed. The addition of a hydroxy-group to a hydroxypteridine has the expected

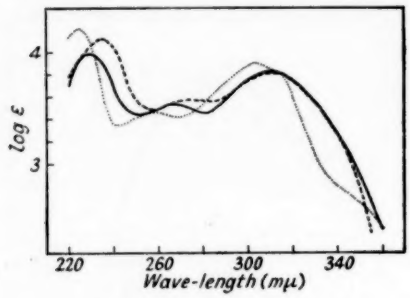


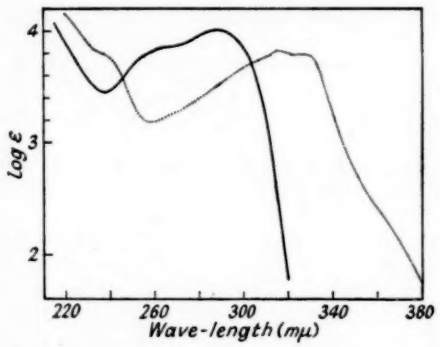
FIG. 4. *Absorption spectra in water of neutral molecules of :*

———— 4-*Hydroxypteridine* (pH 5·6).
. . . . . 4-*Methoxypteridine* (pH 5·7).
– – – – – 3 : 4-*Dihydro*-4-*keto*-3-*methylpteridine* (3-*methyl*-4-*pteridone*) (pH 5·3).

bathochromic effect (see Parts I and II for spectra of 2 : 4- and 6 : 7-dihydroxypteridine; other examples will be published in Part IV). However, in 4-amino-2-hydroxypteridine, the 2-hydroxy-group exerts a large hypsochromic effect on the cation of 4-aminopteridine (Taylor and Cain, *J. Amer. Chem. Soc.*, 1949, **71**, 2538); moreover, Table 3 shows that, in 2-amino-4-hydroxypteridine the 4-hydroxy-group has a strong hypsochromic effect on the neutral molecule of 2-aminopteridine, although not on the cation (see Part I for spectra of monosubstituted pteridines). These two aminohydroxypteridines also have anomalous pK_a values (Table 3). In 4-amino-2-hydroxypteridine, the hydroxy-group is unexpectedly

FIG. 5. *Absorption spectra in water of neutral molecules of :*

———— 6-*Hydroxypteridine* (pH 5·2).
. . . . . 6-*Methoxypteridine* (pH 5·8).



more acidic (9·97 instead of 11·13, as in 2-hydroxypteridine, Part I) but the strength of the amino-group is little changed. On the other hand, in 2-amino-4-hydroxypteridine, the strength of the hydroxy-group is unchanged, but the amino-group has become a much weaker base (2·31 instead of 4·29). The dihydroxypteridines are acids of about the same strength as the stronger of the two monohydroxypteridines from which they are derived (Parts I and II); moreover the only known diaminopteridine (Table 3) is a stronger base than the monoaminopteridines. Hence the examples of acid-strengthening and base-weakening in the aminohydroxypteridines indicate a far-reaching electronic redistribution apparently caused by cross-conjugation. The anomalous spectra support this view, which is of special interest in the case of 2-amino-4-hydroxypteridine, because all naturally occurring pteridines are derivatives of this substance [cf., for example, the abnormally low basic pK_a of xanthopterin (Table 3)].

TABLE 3. *Other physical properties of pteridines.*

Pteridine derivative	pK_a (in water) and concn. at which determined (20°)		R_F [c]	Spectrography in water: $\lambda_{max.}$ (mμ)	Spectrography in water: log $\epsilon_{max.}$ (mol.)	Spectrography in water: pH
2-Methoxy-	—	—	0·80	<220; 325	>4·02; 3·92	6·4
cation	2·13 (±0·09)	M/100	—	—	—	—
4-Methoxy-	—	—	—	225; 258; 304	4·25; 3·45; 3·89	5·7
,,	—	—	—	(226; 262; 301 + 306 + 313 + 319 [g]) [h]	4·17; 3·46; 3·84 + 3·90 + 3·76 + 3·74	—
cation	<1·5	M/30	—	—	—	—
6-Methoxy-	—	—	—	<220; 315 + 327 [g]	>4·14; 3·82 + 3·79	5·8
cation	3·60 (±0·03)	M/100	—	—	—	—
2-Methylamino-	—	—	0·80	229; 273; 388	4·36; 3·96; 3·82	6·5
cation	3·62 (±0·03)	M/100	—	—	—	—
4-Dimethylamino-	—	—	—	241; 362	4·15; 3·93	7·1
cation	4·33 (±0·05)	M/100	—	239; 344 + 347 + 356 [g]	4·19; 4·09 + 4·10 + 4·04	2·0
2-Chloro-	—	—	—	(<220; 302 + 308 + 314 + 322; [g] 378) [h]	>4·05; 3·86 + 3·96 + 3·93 + 3·97; 2·09	—
4-Chloro-	—	—	—	(220; 296 + 303 + 315 [g]) [h]	4·24; 3·86 + 3·92 + 3·82	—
2 : 4-Diamino-	—	—	0·45	—	—	—
cation (mono)	5·32 (±0·03)	M/500	—	—	—	—
cation (di)	<0·5	M/60 [a]	—	—	—	—
2-Amino-4-hydroxy-	—	—	0·40 [f]	270; 340	4·05; 3·76	5·25
cation	2·31 (±0·05)	2×10^{-5}M [b]	—	<220; 315	>4·1; 3·88	0
anion	7·92 (±0·05)	4×10^{-5}M [b]	—	251; 358	4·31; 3·83	13
4-Amino-2-hydroxy-	—	—	0·45	—	—	—
cation	3·21 (±0·09)	M/500 [a]	—	—	—	—
anion	9·97 (±0·03)	M/500 [a]	—	—	—	—
2-Amino-4 : 6-dihydroxy- (xanthopterin)	—	—	0·40 [d]	275; 385	4·12; 3·39	4·93
cation	1·6 (±0·1)	5×10^{-5}M [b]	—	245; 355	4·07; 3·82	(70% H_2SO_4)
anion (mono)	6·3	M/1000 [a]	—	—	—	—
anion (di)	9·23 (±0·04)	M/1000 [a]	—	255; 392	4·27; 3·85	13
4-Hydroxy-6-methyl-	8·19 (±0·02)	M/100	0·55 [e]	—	—	—
4-Hydroxy-7-methyl-	8·09 (±0·02)	M/100	0·50	—	—	—
2-Amino-4 : 6 : 7-trihydroxy- (leucopterin)	—	—	0·05 [f]	(240; 285; 340) [i]	4·20; 3·84; 4·02	13
2 : 4 : 6 : 7-Tetrahydroxy-	—	—	0·05 [f]	(236; 279 + 283 + 286; [g] 347) [i]	4·27; 3·90 + 3·90 + 3·90; 4·03	13
3 : 4-Dihydro-4-keto-3-methyl	<1·3	M/20	—	233; 276; 312	4·12; 3·57; 3·81	5·3

[a] Back-titrated. [b] Determined spectrographically. [c] In butanol–5N-acetic acid (2 : 1) by descending method, 4-hydroxypteridine (R_F = 0·50) being used as a control. When samples of paper contained heavy metals (as shown by their giving more than one spot with 4-hydroxypteridine) a small crystal of sodium sulphide was added to the solvent. Papers viewed in ultra-violet light of 254 mμ. [d] As ammonium salt. [e] Not visible in Wood's light (360 mμ) unless first irradiated at 254 mμ; the 7-methyl isomer is visible directly at either wave-length. [f] As sodium salt. [g] Fine structure. [h] In *cyclo*-hexane to avoid hydrolysis. [i] Poly-anion.

Experimental

M. p.s are uncorrected. The yields of substances that lack a m. p. refer to the stage at which they became chromatographically homogeneous (on paper). Microanalyses were by Mr. P. R. W. Baker, Beckenham.

Solubilities.—Those recorded in Table 1 as " determined spectroscopically " were obtained from initially supersaturated solutions centrifuged for 24 hours after crystals had formed. The maxima of the ultra-violet spectra were compared with those of solutions of known strength. The error should not exceed appreciably that of the instrument, *viz.*, $\pm 1\%$. The other solubilities in Table 1 were determined by inspection, those at 100° being the least amount of water required to dissolve the solid, those at 20° being the least amount of water preventing deposition from a seeded solution. The error here is considered not to exceed $\pm 10\%$. The expression " 1 in 2·5 " means 1 g. in 2·5 ml. of final solution.

Decomposition by Alkali.—Each pteridine (0·001 mole) was heated under reflux with N(or 10N)-sodium hydroxide (10 ml.) at 110° for 1 hour, then steam-distilled in a Kjeldahl apparatus (at constant volume) for 20 minutes. The evolved ammonia was trapped in 0·1N-hydrochloric acid (25 ml.) and back-titrated (methyl-red) with 0·1N-potassium hydroxide (carbonate-free). (In the case of pteridine, which is slightly volatile in steam, this titration was performed potentiometrically, to an end-point of pH 6·0.) The contents of the distillation-flask were then diluted (after neutralization, where necessary) with an appropriate buffer solution to 10^{-4}M. The densities at wave-lengths known to be significant for the starting material, in its various ionic species, were then compared in the " Uvispek " ultra-violet spectrophotometer, of which the solvent cell contained an aqueous solution of the same amount of the same salts brought to the same pH.

Decomposition by Acid.—The pteridines (0·001 mole) were heated as above with N-sulphuric acid (10 ml.). The resulting solution (or suspension) was diluted to 50 ml., of which 25 ml. were transferred to a Kjeldahl apparatus. 10N-Sodium hydroxide (3 ml.) was added and the contents were steam-distilled (at constant volume) for 20 minutes, the evolved ammonia being trapped and back-titrated as above. Both the acidic and the distilled halves of the acid-decomposed solution were examined spectroscopically after preparation as described above. Where a significant difference in the destruction of the two solutions was revealed spectroscopically, it was concluded that alkaline decomposition had occurred during the steam-distillation and hence the titration of ammonia was omitted.

4-Amino-2-methoxy-5-nitropyrimidine.—To a solution from sodium (2·5 g.) in methanol (250 ml.) was added finely ground 4-amino-2-chloro-5-nitropyrimidine (10 g., recrystallized; Part I). The suspension was refluxed with occasional shaking for 90 minutes, then refrigerated overnight. The solid was filtered off, washed by grinding in a mortar with cold water (40 ml.), and dried at 120° (yield 8 g., 82%). A sample, recrystallized from *iso*amyl alcohol (20 parts), gave colourless long needles of *4-amino-2-methoxy-5-nitropyrimidine* with m. p. 203—204° (recovery 90%) (Found : C, 35·5; H, 3·1; N, 33·0. $C_5H_6O_3N_4$ requires C, 35·3; H, 3·5; N, 32·95%).

4-Amino-6-methoxy-5-nitropyrimidine.—4-Amino-6-chloro-5-nitropyrimidine (6·5 g.; Boon, Jones, and Ramage, *J.*, 1951, 96) similarly gave *4-amino-6-methoxy-5-nitropyrimidine* (5·4 g., 85%), m. p. 238—240° (from *iso*butyl methyl ketone) (Found : N, 32·65%).

4-Amino-2-methylamino-5-nitropyrimidine.—4-Amino-2-chloro-5-nitropyrimidine (9·4 g.; see Part I), ethanolic methylamine (33% w/w; 26 ml.), and ethanol (50 ml.) were heated at 100° for 1 hour. After cooling, the product was filtered off, washed with cold ethanol, and dried (yield 8·9 g., 97%). After two recrystallizations of a sample from amyl alcohol (50 parts, with carbon) (80% recovery each time) pale yellow needles of *4-amino-2-methylamino-5-nitropyrimidine*, m. p. 226—228°, were obtained (Found : C, 35·5; H, 4·2; N, 41·2. $C_5H_7O_2N_5$ requires C, 35·5; H, 4·2; N, 41·4%). It is readily soluble in dilute hydrochloric acid, hot amyl alcohol, or chlorobenzene, less soluble in ethanol or water.

4-Amino-6-dimethylamino-5-nitropyrimidine.—Methanolic dimethylamine (14 ml. of 50% w/w solution), methanol (40 ml.), and 4-amino-6-chloro-5-nitropyrimidine (5 g.; Boon, Jones, and Ramage, *loc. cit.*) were heated at 100° for 1 hour. After slow cooling, the long fibrous needles were filtered off (4·5 g., 86%). After three recrystallizations from ethanol (30 parts) pale yellow needles of *4-amino-6-dimethylamino-5-nitropyrimidine* were obtained, m. p. 159—161° (Found : C, 39·2; H, 4·6; N, 38·3. $C_6H_9O_2N_5$ requires C, 39·3; H, 4·9; N, 38·2%).

4 : 5-Diamino-6-chloropyrimidine.—4-Amino-6-chloro-5-nitropyrimidine (4·87 g.) in methanol (320 ml.) was shaken with Raney nickel in hydrogen until 2100 ml. had been absorbed. The

catalyst was filtered off and extracted with boiling methanol. The combined filtrates were taken to dryness. The residue was dissolved in water (120 ml.). This solution was treated with carbon, filtered, and cooled to 0°. 4 : 5-*Diamino-6-chloropyrimidine* was deposited as needles (82%), decomp. *ca.* 248° (Found : C, 33·4; H, 3·3; N, 38·95; Cl, 25·0. $C_4H_5N_4Cl$ requires C, 33·2; H, 3·5; N, 38·8; Cl, 24·5%).

2-*Aminopyrazine-3-carboxymethylamide*.—Methyl 2-aminopyrazine-3-carboxylate (2·0 g.) was shaken with aqueous methylamine solution (25%; 20 ml.) for 10 minutes at room temperature. After a further 30 minutes with occasional shaking, it was chilled for 2 hours and the crystalline material filtered off and dried at 100° (yield 1·7 g., 92%). After two recrystallizations from alcohol (10 parts) 2-*aminopyrazine-3-carboxymethylamide* was obtained as bright yellow needles, m. p. 132—134° (Found : C, 47·4; H, 5·1; N, 37·0. $C_6H_8ON_2$ requires C, 47·35; H, 5·3; N, 36·8%). It was readily soluble in hot water and in organic solvents including boiling light petroleum.

3 : 4-*Dihydro-4-keto-3-methylpteridine*.—2-Aminopyrazine-3-carboxymethylamide (1·6 g.), acetic anhydride (20 ml.), and formic acid (20 ml.) were refluxed for 2 hours, then distilled under vacuum, and the residue was recrystallized from water (12 ml.). The crystals were finely powdered, boiled with alcohol (10 ml.) for 5 minutes, and filtered hot. The insoluble portion was taken up in 200 parts of chloroform (carbon) and filtered. The chloroform was recovered and the residue, recrystallized from 9 parts of water, gave the 4-*pteridone* as creamy-white crystals (0·8 g., 47%), m. p. 286° (Found : C, 51·85; H, 3·6; N, 34·6. $C_7H_6ON_4$ requires C, 51·8; H, 3·7; N, 34·5%). It is decomposed by cold N-hydrochloric acid.

2-*Methoxypteridine*.—Finely powdered crude 4-amino-2-methoxy-5-nitropyrimidine (7 g.), suspended in methanol (150 ml.), was hydrogenated over Raney nickel at room temperature and pressure until about 2·8 l. of hydrogen were consumed (1 hour). The nickel was filtered off and washed with methanol (40 ml.). Dry polyglyoxal (2·9 g.; Part I) was refluxed with the filtrate and washings for 30 minutes. The solution was set aside at room temperature overnight, a small precipitate was discarded, and the filtrate evaporated *in vacuo* at 40° to dryness. The residue was extracted with boiling light petroleum (b. p. 80—100°; 4 × 250 ml.). After refrigeration of the extract, the yellow solid was filtered off (4 g., 52% based on the aminomethoxynitropyrimidine) and recrystallized from light petroleum (200 parts; 90% recovery), then from benzene (6 parts; 83% recovery), giving light yellow needles of 2-*methoxypteridine*, m. p. 149—151°. It is soluble in 35 parts of benzene at 20° and very soluble in cold alcohol (Found : C, 52·15; H, 3·6; N, 34·4. $C_7H_6ON_4$ requires C, 51·85; H, 3·7; N, 34·5%). 2-Methoxypteridine instantly gives a violet colour with cold 10N-hydrochloric acid and a blue colour in boiling 6N-sodium hydroxide.

4-*Methoxypteridine*.—4-Amino-6-methoxy-5-nitropyrimidine (4·7 g.) was suspended in methanol (200 ml.) with Raney nickel and hydrogenated (about 2 l.). The filtered solution was refluxed with polyglyoxal (1·8 g.) for 40 minutes, then evaporated to dryness in a vacuum at 40°. The powdered residue was extracted by refluxing benzene (2 × 100 ml.). The slime that was deposited on standing was filtered off and the filtrate evaporated to dryness in a vacuum (yield 3·4 g., 75%). Three recrystallizations from alcohol (32 parts; charcoal) gave white needles of 4-*methoxypteridine*, m. p. 195° (recovery 80% each time) (Found : C, 51·7; H, 3·65; N, 34·9%), soluble in about 250 parts of alcohol at 0°, and in 40 parts of boiling or 100 parts of cold benzene.

Hydrolysis of Methoxypteridines.—4-Methoxypteridine (0·16 g.; 0·001 mole) was shaken with cold N-sodium hydroxide (2 ml.) for 2 hours. The solution was brought to pH 4 with acetic acid and the liberated 4-hydroxypteridine (0·13 g.; 90%) filtered off. It was identical with specimens prepared by several other methods (see Part I). 2- and 6-Methoxypteridine behaved similarly.

2-*Methylaminopteridine*.—4-Amino-2-methylamino-5-nitropyrimidine (7·7 g.) was hydrogenated in methanol (250 ml.) over Raney nickel (3300 ml.). The nickel was removed and washed with methanol (100 ml.). Polyglyoxal (2·5 g.) was dissolved in the combined filtrates and the solution refluxed for 1 hour, concentrated, and cooled, giving a total yield of 61% of solid. This was recrystallized from alcohol (190 ml.) and then from water (140 ml.; carbon), giving 3·0 g. of 2-*methylaminopteridine*, m. p. 219—220°, as very bright yellow needles, more stable to light than 2-aminopteridine (Part I) (Found : C, 52·5; H, 4·2; N, 43·6. $C_7H_7N_5$ requires C, 52·2; H, 4·4; N, 43·45%), soluble in about 45 parts of boiling alcohol and almost insoluble in benzene. The solution in cold 10N-hydrochloric acid becomes purple in 10 minutes. Boiling 2·5N-sodium hydroxide produces a green colour in 2 minutes.

4-*Dimethylaminopteridine*.—4-Amino-6-dimethylamino-5-nitropyrimidine (3 g.) in methanol (150 ml.) was hydrogenated over Raney nickel at room temperature and pressure (1200 ml.).

The nickel was filtered off, and the filtrate was refluxed with polyglyoxal (1·2 g.) for 30 minutes. After evaporation in a vacuum at 40—45°, the residue was extracted with boiling *cyclo*hexane (3 × 200 ml.). The crystalline material was removed on cooling and the filtrate concentrated to 75 ml., to give a second crop of 4-*dimethylaminopteridine* (70% yield). Recrystallization from light petroleum gave pale yellow needles, m. p. 164—165°, soluble in 650 parts of boiling (and in approx. 4000 parts of cold) light petroleum (b. p. 60—80°), very soluble in water, alcohol, benzene, acetone, and chloroform (Found : C, 54·8; H, 4·8; N, 40·1. $C_8H_9N_5$ requires C, 54·85; H, 5·2; N, 40·0%). Boiling N-sodium hydroxide converts it into 4-hydroxypteridine.

4-*Chloropteridine*.—To 5 : 6-diamino-4-chloropyrimidine (2·15 g.), suspended in phosphate buffer (50 ml. of 1·5M; pH 7·0) at 60°, was added syrupy glyoxal neutralized with sodium hydroxide (2·0 g.; 50% w/w). The mixture was gently agitated until all the solid had gone into solution (about 7 minutes) and heated at 60° for 2 minutes longer. The solution was cooled to 20° and extracted with chloroform (7 × 25 ml.). The dried (Na_2SO_4) chloroform extracts were evaporated in a vacuum. The solid residue (0·57 g.) was extracted with light petroleum (b. p. 60—80°; 350 ml.), and the combined extracts were concentrated to 100 ml. On cooling, yellow needles of 4-*chloropteridine* (0·5 g., 20%) were deposited, decomposing about 140° when placed in a preheated bath (Found : C, 43·8; H, 1·65; Cl, 21·6. $C_6H_3N_4Cl$ requires C, 43·25; H, 1·8; Cl, 21·3%). 4-Chloropteridine darkens on exposure to light and gives a red colour on prolonged boiling in light petroleum.

Azomethine of Glyoxal and 5-*Amino*-4-*hydroxy*-6-*methoxypyrimidine*.—5 : 6-Diamino-4-chloropyrimidine (2·65 g.) and polyglyoxal (1·5 g.) were refluxed in methanol (45 ml.) for 1 hour. The solvent was evaporated in a vacuum and the residue extracted with light petroleum (b. p. 80—100°; 3 × 70 ml.). The filtrate, cooled to 0°, deposited 0·42 g. of yellow chlorine-free crystals. Crystallization from benzene (40 parts; charcoal) gave yellow plates, m. p. 168—169° (Found: C, 47·3; H, 4·0; N, 28·05. $C_{12}H_{12}O_4N_6$ requires C, 47·35; H, 4·0; N, 27·65%). This is consistent with the formulation *glyoxylidenebis*-(5-*amino*-4-*hydroxy*-6-*methoxy*-2-*pyrimidine*). The ultra-violet spectrum shows two well-separated peaks (λ_{max} 250 and 355 mμ; log ε 4·30 and 4·15 respectively). This spectrum resembles those of 1 : 4-diphenylbutadiene, cinnamaldehyde anil, and related substances described by Barany, Braude, and Pianka (*J.*, 1949, 1898). In view of the spectral interchangeability of $^-N{=}$ for $^-CH{=}$ and the bathochromic effects of OH and OMe demonstrated in the paper cited, the spectrum appears to be in good agreement with the formulation.

2 : 4-*Diaminopteridine*.—Crude 2 : 4-diaminopteridine (15 g.), prepared according to Mallette, Taylor, and Cain (*J. Amer. Chem. Soc.*, 1947, **69**, 1814), was suspended in water (200 ml.) at 40°, and 10N-sodium hydroxide (15 ml.) was added with stirring. The suspended solid, now much paler, was filtered off without cooling, washed with cold water, then with ethanol, and dried at 120° (recovery 8·6 g.). Three recrystallizations from boiling water (100 parts, with 0·5 part of carbon) gave 4·3 g. of small, bright yellow needles of chromatographically homogeneous 2 : 4-*diaminopteridine* (Found, after drying at 110° : C, 44·4; H, 3·7; N, 51·7. $C_6H_6N_6$ requires C, 44·4; H, 3·7; N, 51·8%).

4-Amino-2-hydroxypteridine was prepared according to Cain, Mallette, and Taylor (*ibid.*, 1949, **71**, 2538), but recrystallised from water.

4-*Hydroxy*-6-*methylpteridine*.—A mixture of commercial 30% methylglyoxal solution (48 ml.) and sodium hydrogen sulphite solution (*d* 1·34; 120 ml.) was added to a solution of 4-hydroxy-5 : 6-diaminopyrimidine (crude; 16 g.) and sodium sulphite (hydrated; 60 g.) in water (300 ml.) at 60°. The mixture was left at 25—30° for 12 hours. Hydrochloric acid (10N; 100 ml.) was then added and the mixture refrigerated. The resulting yellow complex was filtered off and washed with cold water and then with a little ethanol. When heated at 120° for 45 minutes, this complex lost sulphur dioxide and became grey (11·4 g., 56%). A paper chromatogram at this stage showed the presence of only a trace of the 7-methyl isomer. One recrystallization from water (45 parts; charcoal) gave 8·5 g. of faintly pink but almost pure 4-*hydroxy*-6-*methylpteridine*, free from the 7-isomer. Two further recrystallizations gave a colourless product, decomp. about 345° (Found : C, 52·25; H, 3·7; N, 34·6. $C_7H_6ON_4$ requires C, 51·8; H, 3·7; N, 34·5%).

4-*Hydroxy*-7-*methylpteridine*.—Methylglyoxal (20% solution; 48 ml.) was added to a solution of 4 : 5-diamino-6-hydroxypyrimidine (crude; 16 g.) and sodium sulphite (hydrated; 60 g.) in water (300 ml.) at 90°. The mixture was heated on a water-bath for 10 minutes, then slowly acidified to pH 2 with 10N-hydrochloric acid and cooled to 0°. The crystals were filtered off, washed, and recrystallized from water (9·6 g. of chromatographically homogeneous material). Two more recrystallizations from boiling water (35 parts, with carbon : 75% recovery) produced

long colourless needles of 4-*hydroxy*-7-*methylpteridine*, decomp. >340°, sparingly soluble in boiling amyl alcohol and almost insoluble in other common organic solvents (Found: C, 51·8; H, 3·4; N, 34·8%).

Alkaline Degradation of 4-*Hydroxypteridines*.—4-Hydroxy-7-methylpteridine (0·4 g.) was heated under reflux with 10N-sodium hydroxide (5 ml.) at 140° for 4 hours. Sulphuric acid was added to bring the pH to 2·5. The solution was evaporated and the dry residue was extracted with alcohol. The extract was taken to dryness and the residue was dissolved in one equivalent of alkali, decolorized with carbon, and adjusted to pH 2·5. The crystals which were deposited (70% yield) proved to be 2-amino-6-methylpyrazine-3-carboxylic acid [m. p. 210° (effervescence); cf. 211—212°, Weijlard, Tishler, and Erickson, *J. Amer. Chem. Soc.*, 1945, **167**, 802].

4-Hydroxy-6-methylpteridine (0·8 g.) was heated with 10N-sodium hydroxide (10 ml.) at 140° for 3 hours. The sodium salt which separated on cooling was filtered off and dissolved in hot water (3 ml.). The solution was taken to pH 2·3 with 5N-sulphuric acid and refrigerated, giving 2-amino-5-methylpyrazine-3-carboxylic acid (80%), m. p. 173° (cf. 171—172°, Mowat *et al.*, *ibid.*, 1948, **70**, 14). A mixed m. p. with the above isomeride gave 160°.

6 : 7-*Diethylpteridines*.—Except where otherwise stated the pyrimidine intermediates were prepared as in Part I (*loc. cit.*). 3-Hydroxyhexan-4-one was prepared according to Snell and McElvain (*Org. Synth.*, 1933, **13**, 26) and oxidized to hexane-3 : 4-dione with cupric acetate (Wegmann and Dahn, *Helv. Chim. Acta*, 1946, **29**, 111).

6 : 7-*Diethylpteridine*. 4 : 5-Diaminopyrimidine (0·5 g.; Brown, *J. Appl. Chem.*, 1952, **2**, 239) and hexanedione (0·6 g.) were refluxed in alcohol (10 ml.) for 30 minutes. The solvent was removed at 30—40° in a vacuum and the residue was thoroughly extracted with boiling light petroleum (b. p. 60—80°; 15 ml.). The filtered extract was concentrated to 3 ml.; on cooling, 0·45 g. (53%) of the pteridine crystallized. It was distilled (b. p. 106—108°/0·1 mm.) and gave pale yellow crystals of 6 : 7-*diethylpteridine*, m. p. 50—52° (Found: C, 63·85; H, 6·5; N, 29·8. $C_{10}H_{12}N_4$ requires C, 63·8; H, 6·4; N, 29·8%). Distillation of larger quantities gave poor recovery. It is readily soluble in water and all organic solvents. It slowly becomes pink, particularly in daylight.

2-*Amino*-6 : 7-*diethylpteridine*. Hexanedione (4·15 g.) was added to a warm solution of crude 2 : 4 : 5-triaminopyrimidine (5·5 g.) in water (90 ml.). The mixture was vigorously shaken and heated on the water-bath for 30 minutes with occasional shaking and then refrigerated. Filtration produced 6·0 g. (81%) of a yellow solid, which was recrystallized three times from alcohol (165 parts) with carbon (0·1 part), giving 2-*amino*-6 : 7-*diethylpteridine*, yellow plates, m. p. 230—234° (decomp.) (Found: C, 59·1; H, 6·6; N, 34·15. $C_{10}H_{13}N_5$ requires C, 59·1; H, 6·45; N, 34·45%). It is readily soluble in hot amyl alcohol (with steep temperature gradient), slightly soluble in cold chloroform, but almost insoluble in carbon tetrachloride. The R_F is 0·90 (see Table 3 for method).

4-*Amino*-6 : 7-*diethylpteridine*. Similarly, crude 4 : 5 : 6-triaminopyrimidine (4 g.) and hexanedione (3 g.) gave 4-*amino*-6 : 7-*diethylpteridine*, yellow prisms, decomp. *ca.* 240° (3·8 g., 71%) (from alcohol, 40 parts). It is slightly soluble in chloroform (Found: C, 59·15; H, 6·4; N, 34·0). The R_F is 0·90.

6 : 7-*Diethyl*-2-*hydroxypteridine*. Similarly, 4 : 5-diamino-2-hydroxypyrimidine (4·5 g.; Johns, *Amer. Chem. J.*, 1911, **45**, 79) and hexanedione (4 g.) gave 6 : 7-*diethyl*-2-*hydroxypteridine*, needles, m. p. 155—160° (from alcohol, 45 parts) (6·45 g.) (Found, for material dried at 120°: C, 57·8; H, 7·2; N, 22·35. $C_{10}H_{12}ON_4,C_2H_5{\cdot}OH$ requires C, 57·6; H, 7·25; N, 22·4%). It crystallized from water (100 parts) in tiny rosettes (decomp. about 230°) of the *monohydrate* (Found, for material dried at 80°/15 mm.: C, 54·2; H, 6·2; N, 25·4. $C_{10}H_{12}ON_4,H_2O$ requires C, 54·05; H, 6·35; N, 25·2%). It is slightly soluble in chloroform. The R_F is 0·95.

6 : 7-*Diethyl*-4-*hydroxypteridine*. 5 : 6-Diamino-4-hydroxypyrimidine (4·6 g.) similarly gave 6 : 7-*diethyl*-4-*hydroxypteridine*, needles, m. p. 245° (from alcohol, 30 parts) (5·4 g., 73%), soluble in 20 parts of boiling alcohol and in 350 parts at 0°, slightly soluble in cold chloroform, benzene, or acetone (Found: C, 59·0; H, 5·8; N, 27·0. $C_{10}H_{12}ON_4$ requires C, 58·8; H, 5·9; N, 27·45%). The R_F is 0·85.

2-*Amino*-6 : 7-*diethyl*-4-*hydroxypteridine*. 2 : 5 : 6-Triamino-4-hydroxypyrimidine "bisulphite" (6 g.; Cain, Mallette, and Taylor, *J. Amer. Chem. Soc.*, 1946, **68**, 1998), water (120 ml.), and hexanedione (3 g.) similarly gave 3·5 g. (64%) of cream-coloured product. This was dissolved in cold water (250 ml.) containing sodium hydroxide (2 g.), and the solution stirred with charcoal for 10 minutes, filtered, and adjusted to pH *ca.* 5. The crystals were washed with warm water, dried at 120°, and recrystallized from pure dimethylformamide (200 parts), to give almost white needles of 2-*amino*-6 : 7-*diethyl*-4-*hydroxypteridine* which did not melt below 360°. It is insoluble

in all common solvents, very slightly soluble in boiling pyridine and 2-ethoxyethanol (with steep gradient) (Found: C, 54·5; H, 6·0; N, 31·75. $C_{10}H_{13}ON_5$ requires C, 54·8; H, 6·0; N, 31·95%). The R_F is 0·85.

4-Amino-6 : 7-diethyl-2-hydroxypteridine. 4 : 5 : 6-Triamino-2-hydroxypyrimidine sulphate (6·5 g.; Bendich, Tinker, and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3112) was dissolved in hot water (350 ml.) containing 5N-sulphuric acid (7 ml.). The solution reacted with hexanedione (3 g.) to give faintly yellow needles of *4-amino-6 : 7-diethyl-2-hydroxypteridine*, decomp. about 290° (3·65 g.) (from alcohol, 130 parts), readily soluble in boiling amyl alcohol (with steep gradient) (Found: C, 55·0; H, 5·4; N, 31·55%). The R_F is 0·85.

6 : 7-Diethyl-2 : 4-dihydroxypteridine. 5 : 6-Diamino-2 : 4-dihydroxypyrimidine sulphate (5·2 g.; Bogert and Davidson, *J. Amer. Chem. Soc.*, 1933, **55**, 1667) was dissolved in hot water (130 ml.) containing sodium hydrogen carbonate (3 g.). Hexanedione (3 g.) was added and the reaction effected as before. The pH was adjusted to 2—3 before refrigeration; 3·9 g. (67%) of crystals with m. p. *ca.* 215° were deposited. Two recrystallizations from water (45 parts) gave pale yellow *6 : 7-diethyl-2 : 4-dihydroxypteridine*, m. p. 217—219°, readily soluble in warm alcohol and slightly soluble in chloroform (Found: C, 54·4; H, 6·1; N, 25·2. $C_{10}H_{12}O_2N_4$ requires C, 54·5; H, 5·5; N, 25·45%). The R_F is 0·85.

4-Hydroxy-6 : 7-diphenylpteridine. To a solution of 4 : 5-diamino-6-hydroxypyrimidine (7·0 g.) in hot aqueous alcohol (70 ml.; 50% v/v) was added a hot solution of benzil (10·5 g.) in hot alcohol (350 ml.). The mixture was refluxed on the water-bath for 20 hours (12 hours gave only a 40% yield), refrigerated, and filtered. The crystals were thoroughly stirred with cold acetone (150 ml.) to remove benzil; the yield was 9·25 g. (62%). After recrystallization from *iso*amyl alcohol (85 parts; 90% recovery) cream-coloured needles of *4-hydroxy-6 : 7-diphenylpteridine* were obtained; these softened at 265° and finally melted at 295°. It is slightly soluble in hot alcohol with a steep temperature gradient (Found: C, 71·85; H, 4·0; N, 18·7. $C_{18}H_{12}ON_4$ requires C, 72·0; H, 4·0; N, 18·65%). The R_F is 0·90.

We thank Dr. L. N. Short for the spectrophotometrically-determined pK_a and solubility values and for general supervision of the spectrophotometric work, Mr. E. P. Serjeant for the potentiometric titrations and for skilled spectrophotometric assistance, and Mr. D. T. W. Light for the paper chromatography.

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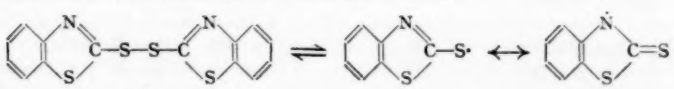
813. 2-*Mercaptobenzothiazole Derivatives. Part I. The Reaction of Di(benzothiazol-2-yl) Disulphide with Olefins.*

By C. G. MOORE.

The reaction of di(benzothiazol-2-yl) disulphide (I) with *cyclo*hexene at 139° yields 2-mercaptobenzothiazole (II), 2-(*cyclo*hex-2-enylthio)benzothiazole (III), and 3-(*cyclo*hex-2-enyl)-2-thiobenzothiazoline (IV). A brief kinetic study of the reaction supports a free-radical chain mechanism. The influence of olefin structure and concentration on the extent and course of the reaction is discussed and, in particular, the reaction of (I) with rubber is considered.

It has been frequently suggested that organic disulphides such as diphenyl disulphide and di(benzothiazol-2-yl) disulphide (I), on being heated in inert solvents, undergo reversible homolysis of the disulphide bond to give RS· radicals, which in the latter case are the mesomeric thiobenzothiazolyl radicals (I*a* ⟷ *b*) :

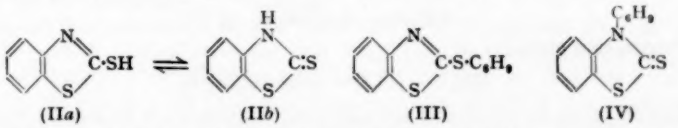


(I) (I*a*) (I*b*)

Evidence for this has been adduced from many experimental sources: *e.g.*, the fact that hot solutions of the disulphides are thermochromic and disobey Beer's law (Schönberg,

Rupp, and Gumlich, *Ber.*, 1933, **66**, 1932; Schönberg and Rupp, *Naturwiss.*, 1933, **21**, 561; Koch, *J.*, 1949, 394, 401), the behaviour on pyrolysis, and the dehydrogenation of benzyl alcohol to benzaldehyde by diphenyl disulphide with formation of thiophenol (Schönberg and Mustafa, *J.*, 1949, 889; *J. Amer. Chem. Soc.*, 1951, **73**, 2401). Ritter and Sharpe's observation (*ibid.*, 1937, **59**, 2351) that disulphides act as effective high-temperature dehydrogenators of hydrocarbons is also best explained on the basis of RS· radical formation. More compelling physicochemical evidence for the coexistence, in equilibrium, of the disulphide (I) and its derived thiobenzothiazolyl radicals (I*a* ⟷ *b*) is that hot solutions of (I) in toluene are paramagnetic (Cutforth and Selwood, *ibid.*, 1948, **70**, 278).

Little work has hitherto been reported on the thermal reaction of (I) and related disulphides with olefins. Farmer and Shipley (see Bloomfield, *J.*, 1947, 1547) showed that 2-mercaptobenzothiazole (II) was a major product of the reaction of (I) with *cyclo*hexene at 140° but no detailed study of the reaction was attempted. Diphenyl disulphide, on the other hand, is entirely without action on this olefin at 180° (Bloomfield, *loc. cit.*). More recently, Barton (*Ind. Eng. Chem.*, 1950, **42**, 671) found 85% reaction of (I) with rubber at 110°, the disulphide appearing as (II). It is of importance that the reaction leading to (II) did not result in cross-linking (vulcanisation) of the rubber.



It has now been found that the reaction of (I) with *cyclo*hexene in the molar ratio of 1 : 10 at 139° gives (II), 2-(*cyclo*hex-2-enylthio)benzothiazole (III), and 3-(*cyclo*hex-2-enyl)-2-thiobenzothiazoline (IV). The physical properties and ultra-violet and infra-red spectra

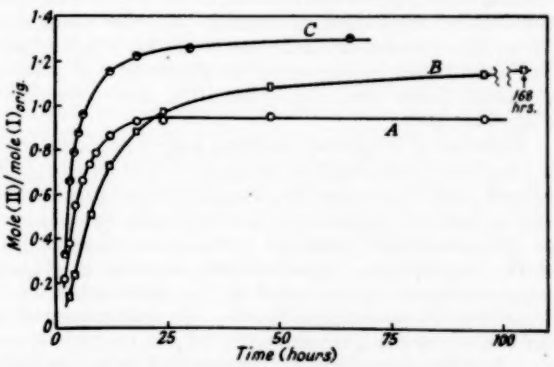
TABLE 1. *Yields of products from the reaction of* (I) (0·01 *mole*) *with* cyclo*hexene* (0·10 *mole*) *at* 139·0° ± 1·0°.

Time (hours)	48·0	96·0
Products (*mole*)	—	—
2-Mercaptobenzothiazole (II)	0·00956	0·00968
2-(*cyclo*Hex-2-enylthio)benzothiazole (III)	0·0052	0·0052
3-(*cyclo*Hex-2-enyl)-2-thiobenzothiazoline (IV)	0·0038	0·0037

A, (I), 1 *mole*; cyclo*hexene*, 10 *moles*; [I], 0·735 *mole l.*$^{-1}$.

B, (I), 1 *mole*; cyclo*hexene*, 2 *moles in benzene*; [I], 0·737 *mole l.*$^{-1}$.

C, (I), 1 *mole*; 1-*methyl*cyclo*hexene*, 10 *moles*; [I], 0·637 *mole l.*$^{-1}$.



of (III) and (IV) thus isolated were very similar to those of synthetic samples. The yields of (II), (III), and (IV) (Table 1; Figure) indicate that under the reaction conditions used the stoicheiometry of the reaction closely follows equation (1);

$$\underset{1\text{ mol.}}{(\text{I})} + \underset{1\text{ mol.}}{\bigcirc} = \underset{1\text{ mol.}}{(\text{II})} + \underset{1\text{ mol.}}{[(\text{III}) + (\text{IV})]} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

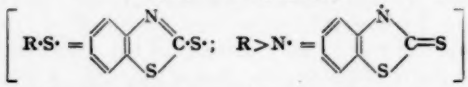
Mechanism of Reaction.—A brief study of the kinetics of the reaction has been made by estimating the yield of (II) as a function of time. The results support the following free-radical chain mechanism:

$$R{\cdot}S{\cdot}S{\cdot}R \xrightarrow{k_1} 2R{\cdot}S{\cdot} \longleftrightarrow 2R{>}N{\cdot} \quad \text{(i)}$$

$$R{\cdot}S{\cdot} \longleftrightarrow R{>}N{\cdot} + C_6H_{10} \xrightarrow{k_1} R{\cdot}SH \rightleftharpoons R{>}NH + C_6H_9{\cdot} \quad \text{(ii)}$$

$$R{\cdot}S{\cdot}S{\cdot}R + C_6H_9{\cdot} \xrightarrow{k_2} \begin{cases} \rightarrow R{\cdot}S{\cdot}C_6H_9\ (III) \\ \rightarrow R{>}N{\cdot}C_6H_9\ (IV) \end{cases} + R{\cdot}S{\cdot} \longleftrightarrow R{>}N{\cdot} \quad \text{(iii)}$$

$$2C_6H_9{\cdot} \xrightarrow{k_4} C_6H_9{\cdot}C_6H_9 \quad \text{(iv)}$$



Application of the stationary-state concept to (i)—(iv) gives:

$$-d[I]/dt = k_1[I] + k_3\sqrt{2k_1/k_4}\,.\,[I]^{3/2} \quad \text{(2)}$$

For *long chains* the first term in (2) becomes negligible and thus:

$$-d[I]/dt = k_3\sqrt{2k_1/k_4}\,.\,[I]^{3/2} \quad \text{(3)}$$

which on integration gives:

$$\{[I]_t^{-\frac{1}{2}} - [I]_0^{-\frac{1}{2}}\} = 0{\cdot}5k_3t\sqrt{2k_1/k_4} \quad \text{(4)}$$

For equation (4) to be applicable the following relation must be closely satisfied:

$$[II]_t = [I]_0 - [I]_t \quad \text{(5)}$$

In the reaction of (I) with *cyclo*hexene the final estimated yield of (II) [0·96—0·97 mole per mole of (I) decomposed] is in agreement with equation (5) and $[I]_t$ can therefore be estimated from it by determining $[II]_t$. When allowance was made for an initial induction period of *ca.* 1 hour a linear plot of $[I]^{-\frac{1}{2}}$ so derived against t was obtained, indicating that the kinetic law (3) holds over an extensive range (*ca.* 20—80%) of the reaction. The composite rate constant, $k_3\sqrt{2k_1/k_4}$, has a value of $9{\cdot}5_5 \times 10^{-5}$ mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$ at 139·0° ± 1·0°.

The fact that (III) and (IV) readily undergo mutual thermal isomerisation at 139°, leading to an equilibrium mixture of the two isomers (see Part II), prevents a decision as to the detailed mechanism of reaction (iii). Two radical substitution reactions are possible: (*a*) an S_R2 mechanism, analogous to the ionic S_N2 substitution, leading to (III); and (*b*) an S_R2' mechanism, analogous to the abnormal S_N2' substitution (Young, Webb, and Goering, *J. Amer. Chem. Soc.*, 1951, **73**, 1076, and references therein), leading to the isomeric compound (IV).

Influence of Reaction Conditions and Olefin Structure on $[II]_{max.}$.—Inspection of the data in the Figure indicates that the final yield of 2-mercaptobenzothiazole, $[II]_{max.}$, is dependent on both the reaction conditions and the structure of the olefin. Thus, reaction of (I) (1 mol.) with *cyclo*hexene (2 mols.) in benzene under disulphide concentration conditions equivalent to the non-diluted mixture raised the value of $[II]_{max.}$ to *ca.* 1·18 mole per mole of (I) decomposed. Whether this increase in $[II]_{max.}$ is due to the decreased olefin concentration or is the result of the intervention of benzene in the reaction cannot be decided on the available evidence. On replacement of *cyclo*hexene by 1-methyl*cyclo*hexene the change in the stoicheiometry of the reaction is even greater, a value of $[II]_{max.}$ = *ca.* 1·3 mole per mole of (I) decomposed being attained. These findings reveal that the rate equation (3) is no longer applicable in these cases. However, they are not necessarily inconsistent with the mechanism (i)—(iv) but may reflect an increase in the importance of the termination step (iv) compared with the second propagation step (iii), leading to a propagation sequence of short chain-length and the necessity to retain the first term in (2). No final statement as to the applicability or otherwise of the mechanism (i)—(iv) or the importance of the termination step (iv) can be made on the basis of the present data.

Barton's observation (*loc. cit.*) that the reaction of (I) with rubber does not lead to appreciable cross-linking (vulcanisation) suggests that the reported high value of $[II]_{max.}$ [1·7 mole per mole of (I) decomposed] is not the result of the increased importance of alkenyl-radical dimerisation (iv), a reaction tantamount to cross-linking of the rubber. Barton interprets the reaction as a dehydrogenation of the polyisoprene by (I) according to (6):

$$R'H_x + R{\cdot}S{\cdot}S{\cdot}R = R'H_{(x-2)} + 2R{\cdot}SH \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

It is reasonable to argue that polyisoprenyl radicals will be formed as the result of a reaction similar to (i) but not that these radicals will lead to a dehydrogenated rubber directly. This follows from the recent observation by Farmer and Moore (*J.*, 1951, 131, 142) that polyisoprenyl and related alkenyl radicals derived from the parent olefins by the action of *tert.*-butoxy-radicals at 100—140° participate almost entirely in coupling reactions, *e.g.*:

$$Bu^tO{\cdot} + {-}CH_2{\cdot}CH{=}CH{-} \longrightarrow Bu^tOH + {-}\dot{C}H{\cdot}CH{=}CH{-}$$
$$2\,{-}\dot{C}H{\cdot}CH{=}CH{-} \longrightarrow {-}CH{\cdot}CH{=}CH{-}$$
$$\phantom{2\,{-}\dot{C}H{\cdot}CH{=}CH{-} \longrightarrow} {-}\dot{C}H{\cdot}CH{=}CH{-}$$

The close similarity in conditions of radical production in these and in Barton's experiments makes it most improbable that there would be a major change in radical reactivity in the two systems.

The apparent inconsistencies can be reconciled if it is assumed (*a*) that the chain-mechanism (i)—(iv) is applicable in the case of rubber, (*b*) that the chain-length is long, leading to a minimum of cross-linking according to (iv), and (*c*) that the yield of (II) in considerable excess of 1 mole per mole of (I) decomposed is the result of a secondary thermal decomposition of the primarily formed polyisoprenyl analogues of (III) and (IV) leading to (II) and the dehydrogenated rubbber. The last assumption is consistent with the known ability of (III) and (IV) and related compounds to undergo thermal decomposition, leading to (II), as an alternative reaction to their mutual thermal isomerisation (Part II). The relative importance of the thermal decomposition reaction evidently depends on both the reaction temperature and the nature of the alkenyl substituent and it may well be that in the case of the polyisoprenyl analogues of (III) and (IV) the configurational conditions favour predominance of the decomposition.

Experimental

Materials.—*cyclo*Hexene, freshly distilled from sodium before use, had b. p. 82·5—82·7°/758—762 mm., n_D^{20} 1·4470 (Found: C, 87·8; H, 12·1; O, 0·12. Calc. for C_6H_{10}: C, 87·7; H, 12·3%); Infra-red analysis showed the absence of carbonyl and hydroxyl groups. 1-Methyl*cyclo*hexene had b. p. 109·2°/764 mm., n_D^{20} 1·4509 (Found: C, 87·2; H, 12·5; O, <0·1. Calc. for C_7H_{12}: C, 87·4; H, 12·6%). A commercial sample of di(benzothiazol-2-yl) disulphide (I), crystallised from benzene, had m. p. 178·5—179°. A sample of (I) prepared from pure (II) by iodine oxidation crystallised from benzene in colourless plates, m. p. 180—181° (Found: C, 50·8; H, 2·55; N, 8·4; S, 38·45. Calc. for $C_{14}H_8N_2S_4$: C, 50·6; H, 2·4; N, 8·4; S, 38·6%). Ultra-violet analysis showed that both samples contained <1% of (II).

Reaction of Di(benzothiazol-2-yl) Disulphide (I) *with* cyclo*Hexene.*—(*a*) The olefin (41·0 g., 0·5 mole) and the disulphide (16·60 g., 0·05 mole) were heated at $<10^{-3}$ mm. in a Carius tube at 139·0° ± 0·5° for 24·0 hours. After removal of unchanged olefin the product (19·55 g.) was dissolved in chloroform (200 ml.) and extracted with 10% aqueous sodium hydroxide (3 × 100 ml.). The first 200 ml. of alkaline extract on acidification (concentrated hydrochloric acid, 60 ml.) gave (II) (7·44 g., 0·0445 mole), which after crystallisation from water or ethanol had m. p. and mixed m. p. with an authentic sample, 179—180° (Found: C, 50·3; H, 3·1; N, 8·5; S, 38·7%; equiv., 168·0, 169·0. Calc. for $C_7H_5NS_2$: C, 50·3; H, 3·0; N, 8·4; S, 38·35%; equiv., 167·2). Acidification of the final 100 ml. of extract gave no further (II) showing that complete extraction of the thiol had been effected. The chloroform solution, after being washed with water, dried ($CaCl_2$), and freed from solvent, gave an orange viscous liquid (12·07 g.) which was rapidly distilled at as low a temperature as possible, giving as main fraction a light yellow oil, b. p. 140—170° (mainly 162—170°)/0·005 mm. (6·9 g.), which partly crystallised on storage. Separation of the mixture gave a filtrate (i) (4·7 g.), n_D^{20} 1·668, and a residue (ii) (2·2 g.).

The filtrate (i) consisted mainly of 2-(cyclo*hex*-2-*enylthio*)*benzothiazole* (III) together with *ca.* 4% of (II) and *ca.* 6% of 3-(cyclo*hex*-2-*enyl*)-2-*thiobenzothiazoline* (IV) (Found: C, 62·4;

H, 5·3; N, 5·8, 5·9; S, 26·25. $C_{13}H_{13}NS_2$ requires C, 63·1; H, 5·3; N, 5·7; S, 25·9%). Extraction of a portion (2·37 g.) of (i) in chloroform (50 ml.) with 10% aqueous sodium hydroxide (25 ml.) gave (II) (0·047 g., *i.e.*, 2%), m. p. 177—178°, mixed m. p. 177—178·5°. The alkali-insoluble portion, on removal of the solvent, gave almost pure (III) (2·21 g.), n_D^{20} 1·665 (Found: C, 62·8; H, 5·35; N, 6·2; S, 26·15%). The ultra-violet and infra-red spectra of this sample were identical with those of a synthetic sample of (III); a shoulder at ~3290 Å may be due to *ca.* 6% of (IV).

The residue (ii) was triturated with concentrated hydrochloric acid to remove traces of (III), and the resultant crystalline solid (2·1 g.) on alkali-extraction gave (II) (0·274 g.), m. p. and mixed m. p. 177—178°. The alkali-insoluble product (1·76 g.) was 3-(*cyclo*hex-2-enyl)-2-thiobenzothiazoline (IV) which crystallised from ethanol in light yellow prisms, m. p. and mixed m. p. with synthetic sample, 148·0° (Found: C, 63·15; H, 5·3; N, 5·9; S, 25·6%). The ultra-violet and infra-red spectra were identical with those of the synthetic sample.

The residue (5·02 g.) from the original distillation was shown by alkali-extraction to contain (II) (0·41 g.). The resultant alkali-insoluble product (4·55 g.) was a deep orange-brown oil which was not further examined.

(*b*) The olefin (8·21 g., 0·10 mole) and the disulphide (3·32 g., 0·01 mole) were heated at 139·0° ± 0·5° for (i) 48·0 and (ii) 96·0 hours. After removal of the unchanged olefin, (II) was quantitatively extracted with aqueous sodium hydroxide by the method described below. The alkali-insoluble product, after removal of the chloroform, was weighed, made up to a standard solution in ethanol, and analysed for (III) and (IV) by the ultra-violet spectrometric method described in Part II. The yields of the various products are given in Table 1.

Synthesis of 2-(cyclo*Hex*-2-*enylthio*)*benzothiazole* (III) and 3-(cyclo*Hex*-2-*enyl*)-2-*thiobenzothiazoline* (IV).—(*a*) A methanolic solution of 2-sodiothiobenzothiazole was made from anhydrous sodium methoxide (28·7 g., 0·53 mole) and (II) (88·9 g., 0·53 mole) under nitrogen. The methanol was replaced by pure toluene and to the resultant suspension, held at 80—90°, was added 3-bromo*cyclo*hexene (100·0 g., 0·62 mole; b. p. 57—58°/12 mm., n_D^{20} 1·5271) during 0·5 hour. After reaction for a further 6 hours at 80—90° the mixture was poured into water, and the toluene layer separated, extracted with 10% aqueous sodium hydroxide, washed with water, and finally dried ($CaCl_2$). Removal of the solvent and distillation of the product gave a mixture of (III) and (IV) (77·0 g., 59%), b. p. 157—159°/0·1 mm., as a light-yellow oil, which partly crystallised during one week under nitrogen. The solid was filtered off, washed with concentrated hydrochloric acid and then water, and extracted with alkali to remove (II) formed in the distillation. Crystallisation of the resultant solid from ethanol gave pure (IV) (27·6 g.) as light-yellow prisms, m. p. 148·0° (Found: C, 63·05; H, 5·35; N, 5·5; S, 25·75%). The filtrate, after similar extraction with alkali, gave (III) (30·1 g.; n_D^{20} 1·6666) containing 4·8% of (IV) [Found: C, 63·0; H, 5·25; N, 5·75; S, 25·75%; Light absorption (in ethanol): max. 2820, 2910, 3010 Å; ε, 13,120, 12,540, 11,000 respectively; $E^{1\%}_{1\text{ cm. }2815}$, 527·5; $E^{1\%}_{1\text{ cm. }3265}$, 52·8]. On the basis of these values $E^{1\%}_{1\text{ cm. }2815} = 550{\cdot}0$ for pure (III).

(*b*) The same compounds were obtained by treating 2-sodiothiobenzothiazole [from (II), 75·2 g., 0·45 mole; sodium methoxide, 24·3 g., 0·45 mole] in ethanol (100 ml.) with the bromide (75·8 g., 0·47 mole) at 85° for 2·0 hours under nitrogen. The concentrations of the reactants (sodio-salt ~2·3M; bromide ~2·4M) were those conducive to an S_N2 reaction. The product, worked up as described above, gave (III) (26·2 g., 24%), n_D^{20} 1·6659 [Found: C, 63·1, 63·05; H, 5·3, 5·35; N, 5·7; S, 25·75%; Light absorption (in ethanol): $E^{1\%}_{1\text{ cm. }2815}$, 522·3; $E^{1\%}_{1\text{ cm. }3265}$, 61·0], containing 5·6% of the isomer (IV). On the basis of this value the $\varepsilon_{max.}$ and $E^{1\%}_{1\text{ cm.}}$ values for pure (III) are $\varepsilon_{2820} = 13{,}600$; $\varepsilon_{2910} = 12{,}940$; $\varepsilon_{3010} = 11{,}160$; $E^{1\%}_{1\text{ cm. }2815} = 548{\cdot}3$. The pure (IV) (14·4 g., 13%) had m. p. 147—148° [Found: C, 63·0; H, 5·45; N, 5·8; S, 25·7%; Light absorption (in ethanol): max. 2420, 3270 Å; $\varepsilon_{2420} = 12{,}640$; $\varepsilon_{3270} = 26{,}200$; $E^{1\%}_{1\text{ cm. }2815}$, 88·8; $E^{1\%}_{1\text{ cm. }3265}$, 1058].

Reaction Kinetics.—(a) *Estimation of* 2-*mercaptobenzothiazole* (II). The sample for analysis of (II) was dissolved in chloroform (100 ml.), cooled to 0°, and extracted, by vigorous shaking for 10 minutes, with 10% aqueous sodium hydroxide (25·0 ml.). The alkaline extract was separated, the separating funnel was washed with water (2 × 5 ml.) followed by concentrated hydrochloric acid (15 ml.), and both washings were added to the alkaline extract. Next morning the precipitated (II) was filtered off (Gooch), washed with water (3 × 5 ml.), and dried to constant weight at 100—120°. The representative results given in Tables 2 and 3 indicate the applicability of the above procedure for estimation of (II) in the range 0·4—2·3 g. in admixture with (I), (III), and (IV).

(b) *Reaction of* (I) *with* cyclo*hexene*. The disulphide and the olefin were heated at

TABLE 2.

(II) (g.)	Recovery of (II) (%)	(II) (g.)	Recovery of (II) (%)	(II) (g.)	Recovery of (II) (%)	(II) (g.)	Recovery of (II) (%)
0·1006	93·9	0·6036	98·5	1·3002	99·2	1·9899	99·8
0·1882	96·7	0·8016	98·4	1·6212	99·2	2·2740	99·6
0·4018	98·2	1·0060	98·9	1·7162	99·2	—	—

TABLE 3.

(II) (g.)	(I) (g.)	(III) (g.)	(IV) (g.)	Recovery of (II) (%)
0·3890	1·5353	—	—	100·4
0·5875	1·0865	—	—	99·1
1·2274	0·5571	—	—	101·1
1·4244	0·3225	—	—	99·8
0·5003	2·3192	0·3704	0·3697	102·3
0·8300	1·6606	0·6196	0·6182	101·4
1·3396	0·6566	0·9912	0·9892	101·1
1·6710	—	1·2290	1·2308	99·6

TABLE 4. *Reaction of* (I) (3·32 *g.*, 0·01 *mole*) *with* cyclo*hexene* (8·21 *g.*, 0·10 *mole*) *at* 139·0° ± 1·0°. *Concn. of* (I), 0·735 *mole l.*$^{-1}$

Time (hours)	2·0	3·0	4·5	6·0	7·5	9·0	12·0	18·0	24·0	48·0	96·0
[II], mole l.$^{-1}$	0·160	0·279	0·402	0·486	0·539	0·578	0·637	0·686	0·690	0·705 *	0·703 †

* Mean of three determinations. † Mean of five determinations.

$<10^{-3}$ mm. and 139·0° ± 1·0° for the appropriate time. It was necessary to shake the reactants for the first hour to effect solution of the disulphide. The product, after removal of the unchanged olefin, was analysed for (II) by the procedure described above. The yields of (II) are given in Table 4 and the Figure.

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814. 2-*Mercaptobenzothiazole Derivatives. Part II.* The Thermal Decomposition and Isomerisation of 2-Alkyl- and 2-Alkenyl-thiobenzothiazoles and 3-Alkyl- and 3-Alkenyl-2-thiobenzothiazolines.*

By C. G. MOORE and E. S. WAIGHT.

A study of the thermal treatment of variously constituted 2-alkyl- and 2-alkenyl-thiobenzothiazoles (I) and 3-alkyl- and 3-alkenyl-2-thiobenzothiazolines (II) reveals that two reaction courses are operative: (i) the thermal isomerisation of (I) to (II), which is reversible when R = alkenyl; and (ii) the thermal decomposition of (I) to 2-mercaptobenzothiazole (III) and a hydrocarbon derived from R by loss of hydrogen. Examples of the sole operation of (i) and (ii) are found in the cases of (I; R = allyl, *cyclo*hexyl respectively). All the other compounds studied show mixed reaction characteristics. A kinetic study of the decomposition or reversible isomerisation of (I; R = *cyclo*hexyl, allyl, and *cyclo*hex-2-enyl) indicates that the reactions are of the first order. The mechanisms of the decompositions and isomerisations are discussed and the relation of the reversible isomerisations of (I) and (II) (R = alkenyl) to the Claisen and analogous rearrangements is detailed.

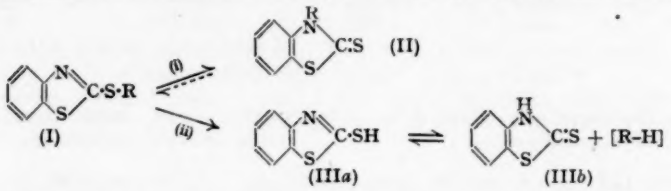
THE isolation of 2-(*cyclo*hex-2-enylthio)benzothiazole (I; R = *cyclo*hex-2-enyl) and 3-(*cyclo*hex-2-enyl)-2-thiobenzothiazoline (II; R = *cyclo*hex-2-enyl) in equilibrium proportions (Part I *) necessitated a study of the pyrolysis of these and related compounds in order to determine the factors influencing their relative tendencies towards isomerisation and decomposition.

This paper is concerned with the thermal treatment of compounds of types (I) and (II) in which the substituent R is alkyl, aralkyl, and alkenyl. Previous studies in this field have

* Part I, preceding paper.

been made by Reed, Robertson, and Sexton (*J.*, 1939, 473) and by Fry and Kendall (*J.*, 1951, 1723). In the present work the reactions were studied under carefully controlled experimental conditions and in the cases of (I; R = *cyclo*hexyl, *cyclo*hex-2-enyl, and allyl) the kinetics of the reactions were studied, thus permitting worthwhile discussion of the reaction mechanisms.

Table 1 summarises the yields of (I), (II), and (III) obtained on heating (I), containing differently constituted substituents R, for 48 hours at 200°. Since melts of the pure sulphides were used the initial concentrations of the reactants vary slightly, but without significance for the present purpose. Two reaction courses are obviously operative: (i) thermal isomerisation of (I) to (II), which is reversible when R = allyl, *trans*-but-2-enyl, and *cyclo*hex-2-enyl; and (ii) thermal decomposition of (I) to 2-mercaptobenzothiazole (III) and a hydrocarbon derived from R by the loss of hydrogen. As examples of (ii) may



be cited (I; R = *cyclo*hexyl) which gives (III) and *cyclo*hexene, and (I; R = benzyl) which gives (III) and *trans*-stilbene [cf. Reed *et al.*, *loc. cit.*, who reported (II; R = benzyl) as the sole product of the iodine-catalysed pyrolysis of (I; R = benzyl) at 200°].

The relative importance of reactions (i) and (ii) and their absolute rates are seen to be

TABLE 1. *Thermal isomerisation and decomposition of* (I) (200° ± 2°, 48·0 *hours*).

[Yields: Mole % of (I), (II), and (III).]

Substituent R	Mole % (I)	Mole % (II)	Mole % (III)
Methyl	98	2	0·15
n-Octyl	96·5	0·9	~1
*iso*Propyl	83·5	2	13·0
*cyclo*Hexyl	90	0	7·7
Benzyl	~76	3·5	20·1
Allyl †	11	87	0
trans-But-2-enyl (20·0 hours)	55	41·5	2
,, (48·0 hours) *	28	65·5	3·7
,, (48·0 hours) §	32	63	3·7
*cyclo*Hex-2-enyl ‡	23·5	40·5	34·2

* Results of micro-scale experiment. † Equilibrium mixture.
‡ Apparent equilibrium mixture. § Results of macro-scale experiment.

critically dependent on the nature of R. An extreme case of the sole operation of (i) is found in (I; R = allyl) where no detectable amount of (III) is formed. An extreme case of the sole operation of (ii) is exemplified by (I; R = *cyclo*hexyl) where only a negligible amount (<0·2 mole %) of (II; R = *cyclo*hexyl) was found (see Experimental section). The relative facility of (ii) is seen to vary with the nature of R thus: primary alkyl < *sec.*-alkyl < aralkyl; and the change is also sensitive to slight structural changes in the alkenyl groupings thus: allyl < *trans*-but-2-enyl ≪ *cyclo*hex-2-enyl.

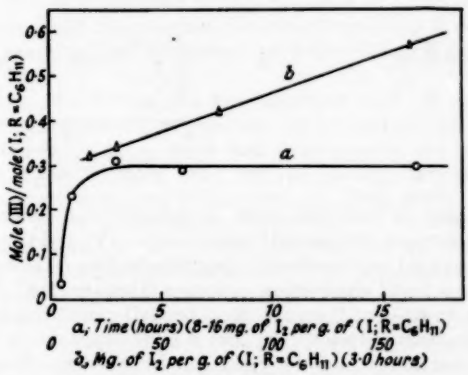
The reaction course of (I; R = *cyclo*hexyl) was uninfluenced by temperature within the range 200—230° and of (I; R = allyl) within the range 140—200°. In the case of (I) and (II) (R = *cyclo*hex-2-enyl), however, although at 110—140° the reversible isomerisation (i) suffered negligible contamination with (ii), at 200° (ii) intruded to a considerable extent. An unusual feature of the latter decomposition was that the volatile product originating from the *cyclo*hex-2-enyl grouping consisted mainly of benzene and *cyclo*hexene, the expected olefin, *cyclo*hexa-1 : 3-diene, being only a very minor constituent. A second unusual and unexplained feature of the 200° reaction is that an apparent equilibrium state is reached between the various products (see Experimental, Table 11).

The Iodine-Catalysed Decomposition of (I; R = cyclo*Hexyl*).—Contrary to its catalysis of the *isomerisation* of (I; R = Me and Et) to (II; R = Me and Et, respectively) (Reed

et al., loc. cit.) iodine acts as an efficient catalyst for the *decomposition* of (I; R = *cyclo*hexyl) at 200° into (III) and *cyclo*hexene. Reaction conditions leading to the formation of ~30 mole % of (III) also yielded (II; R = *cyclo*hexyl) (4·6 mole %), a result in contrast with the absence of this product in the uncatalysed decomposition. The effects of reaction time and catalyst concentration on the yield of (III) are given in Fig. 1 and indicate (*a*) that for a constant initial iodine concentration (8—16 mg. of iodine per g. of sulphide) the yield of (III) reaches a maximum of ~30 mole %, and (*b*) that the yield of (III) after three hours' reaction is a linear function of the initial iodine concentration. The former result suggests that the catalyst is consumed during the reaction.

Reaction Kinetics.—The kinetics of the decomposition or reversible isomerisation have been investigated for (I; R = *cyclo*hexyl, allyl, and *cyclo*hex-2-enyl) under temperature conditions chosen to give a single reaction course, *i.e.*, the decomposition route (ii) for (I; R = *cyclo*hexyl) and the reversible isomerisation (i) for (I; R = allyl and *cyclo*hex-2-enyl).

FIG. 1.



The initial rates of 2-mercaptobenzothiazole formation from (I; R = *cyclo*hexyl) at 230° were measured at several concentrations, with diphenyl as an inert diluent. The first-order nature of the reaction is apparent from the linear initial rate–initial concentration relation. There were indications of deviation from the first-order law with increasing decomposition, possibly owing to the reversibility of the process or to environmental effects arising from the increasing accumulation of products. Rate constants determined for the decomposition of the pure sulphide in the temperature range 200—230° yielded a linear Arrhenius plot (E = 43·5 kcal. mole^{-1}).

The reversible isomerisations of (I) and (II) (R = allyl and *cyclo*hex-2-enyl) were studied quantitatively by an ultra-violet spectrometric method (see Experimental). The excellent linear plots which were obtained of $\log_{10}[E^{1\%}_{1\text{ cm. }3265_e} - E^{1\%}_{1\text{ cm. }3265_t}]$ against time indicate that these isomerisations obey the kinetic law governing a reversible first-order reaction over an extensive range of reaction. Since the sum of the velocity constants for the forward (k_1) and reverse (k_2) reactions is obtainable from the slopes of the lines, and the ratio from the equilibrium concentrations of (II; R = allyl and *cyclo*hex-2-enyl), as estimated from the maximum $E^{1\%}_{1\text{ cm. }3265}$ values attained, k_1 and k_2 can readily be evaluated separately (Tables 2 and 3). The derived activation energies are given in Table 4.

TABLE 2. *Reversible isomerisation of* (I) *and* (II) (R = allyl).

		Mole %				
Temp. (° K)	$10^6(k_1 + k_2)$ (sec.$^{-1}$)	$(I)_e$ *	$(II)_e$	k_1/k_2	10^6k_1 (sec.$^{-1}$)	10^6k_2 (sec.$^{-1}$)
413 ± 0·1	2·78	6·9	93·1	13·5	2·59	0·19
433 ± 0·5	16·5	7·8	92·2	11·7	15·2	1·3
453 ± 0·5	82·1	9·2	90·8	9·9	74·4	7·7
473 ± 1·0	350	12·1	87·9	7·2	310	40

* Taken as 100 − mole % $(II)_e$.

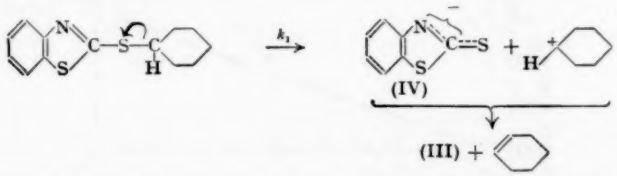
TABLE 3. *Reversible isomerisation of* (I) *and* (III) (R = *cyclo*hex-2-enyl).

Temp. (° K)	Initial concn. of (I) (mole $l.^{-1}$)	$10^6(k_1 + k_2)$ ($sec.^{-1}$)	Mole % (I)$_e$ *	Mole % (II)$_e$	k_1/k_2	10^6k_1 ($sec.^{-1}$)	10^6k_2 ($sec.^{-1}$)
383 ± 0·2	—	7·61	18·0	82·0	4·56	6·24	1·37
398 ± 0·2	—	33·4	21·4	78·6	3·67	26·2	7·2
413 ± 0·2	4·6	134	25·6	74·4	2·91	100	34
,,	0·36 †	65	45·6	54·4	1·19	35	30
,,	0·034 †	56	48·1	51·9	1·08	29	27

* Taken as 100 − mole % (II)$_e$. † *cyclo*Hexene as diluent.

The equilibrium proportions of (I) and (II) (R = allyl) were also determined with (II; R = allyl) as the initial reactant. The results (see Experimental, Table 12) confirm that the reaction is truly reversible.

Discussion of Reaction Mechanisms.—(1) *The mechanism of the decomposition reaction* (ii). The accumulated evidence suggests that the decomposition of (I) to (III) and (R–H) is ionic in nature. Thus, for (I; R = *cyclo*hexyl), we envisage:

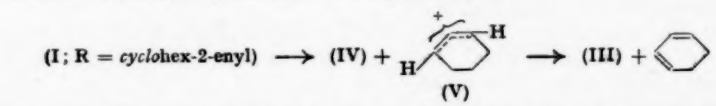


The rate-determining step is identified with a unimolecular heterolytic fission of the C–S bond to give the mesomeric thiobenzothiazolyl anion (IV) and the *cyclo*hexylcarbonium ion, being followed by a rapid proton-transfer reaction to give (III) and *cyclo*hexene. The reaction is thus analogous to *E*1 elimination processes (Hughes *et al.*, *J.*, 1948, 2038 *et seq.*).

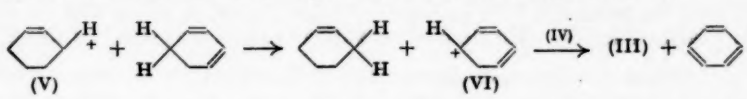
The formation of *trans*-stilbene from (I; R = benzyl) cannot be accounted for directly by a proton-transfer reaction between (IV) and a benzylcarbonium ion. However, it is possible that such a reaction occurs to yield the benzylidene diradical which is then stabilised by dimerisation to *trans*-stilbene (cf. Bickel and Waters, *Rec. Trav. chim.*, 1950, **69**, 312):

$$\text{(I; R = benzyl)} \xrightarrow{k_1} \text{(IV)} + C_6H_5{-}CH_2^+ \longrightarrow \text{(III)} + C_6H_5{-}\dot{C}H \xrightarrow{\text{Dimerisation}} \underset{trans}{C_6H_5{\cdot}CH{=}CH{\cdot}C_6H_5}$$

The formation of *cyclo*hexene and benzene as the major products of the thermal decomposition of (I; R = *cyclo*hex-2-enyl) is in accord with the known behaviour of carbonium ions. The primary reactions are envisaged as:



the *cyclo*hexene and benzene then resulting from the interaction of the carbonium ion (V) with the *cyclo*hexa-1 : 3-diene (cf. Bartlett, Condon, and Schneider, *J. Amer. Chem. Soc.*, 1944, **66**, 1531; Schneider and Kennedy, *ibid.*, 1951, **73**, 5013, 5017, 5024):



The driving force of the reaction is the greater resonance stabilisation of (VI), containing the mesomeric pentadienyl-ion system ($R{\cdot}\overset{+}{C}H{=}CH{=}CH{=}CH{=}\overset{+}{C}H{\cdot}R'$), compared with the resonance stabilisation of the allyl ion system ($R{\cdot}\overset{+}{C}H{=}CH{=}\overset{+}{C}H{\cdot}R'$) present in (V).

The carbonium ions might be expected to cause some polymerisation of the olefinic products and in fact evidence for the formation of a hydrocarbon polymer was obtained. Additional support for the utilisation of some of the *cyclo*hexene in this way is provided by the preponderance of benzene in the isolated hydrocarbon mixture.

Two factors responsible for the relative facility of decomposition of (I), with different substituents R, can now be considered: (*a*) the rate of unimolecular heterolytic fission of the relevant C–S bond; and (*b*) the ease of removal of a proton from the derived carbonium ion. The first of these depends on the resonance stabilisation energy of the carbonium ion R^+ and is therefore expected to be facilitated by substitution as follows:

$$R^+_{\text{prim. alkyl}} < R^+_{\text{sec.-alkyl}} < R^+_{\text{aralkyl}} \sim R^+_{\text{alkenyl}}$$

This is the order observed experimentally for the ease of decomposition of (I) when this is the sole or major reaction. The intrusion of the second factor (*b*) becomes apparent when the relative rates of the decomposition (ii) and isomerisation (i) processes for a given compound are considered. The greater the ease of loss of a proton from R^+ the less will (i) compete with (ii). The extreme case of this is where $R^+ = C_6H_{11}^+$ and (ii) is the sole reaction; on the other hand the observed isomerisation of (I; R = Me) to (II; R = Me) as the predominant reaction is in agreement with the expected difficulty of removal of a proton from Me^+.

The catalytic action of iodine on the decomposition of (I; R = *cyclo*hexyl) is regarded as resulting from the formation of a sulphonium salt of the type $RR'SI^+\}I^-$, which increases the polarisation of the $S–C_{(cyclohexyl)}$ bond and consequently its ease of dissociation (see Tarbell and Harnish, *Chem. Reviews*, 1951, **49**, 1). Iodine-catalysis of the dehydration of alcohols has been similarly explained (Dhar *et al.*, *J.*, 1948, 2093).

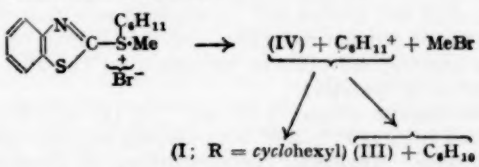
(2) *The mechanism of the isomerisation reaction* (ii). It is convenient to consider two groups of compounds separately: (*A*) (I; R = alkyl and aralkyl) and (*B*) (I; R = alkenyl).

(*A*) *2-Alkyl- and 2-aralkyl-thiobenzothiazoles.* The isomerisation of these sulphides to the more thermally stable thiazoline derivatives (II; R = alkyl and aralkyl) is believed to proceed *via* the intermediate formation of the mesomeric thiobenzothiazolyl anion and the relevant carbonium ion, the rate-determining step again being the unimolecular heterolytic fission of the C–S bond. The isomerisation thus becomes an alternative to the decomposition reaction (ii), and is subject to the same governing factors (*a* and *b* above):

$$\text{(I; R = alkyl or aralkyl)} \longrightarrow \text{(IV)} + R^+ \xrightarrow{\text{(ii)}} \text{(II; R = alkyl or aralkyl)}$$

Iodine and bromine presumably catalyse these isomerisations (Reed *et al.*, *loc. cit.*) just as they do the decomposition of (I; R = *cyclo*hexyl) (see above), but the similar action of alkyl halides is not so clear.

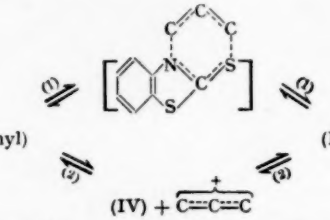
It has now been found that when (I; R = Me) is heated with *cyclo*hexyl bromide at 200° methyl bromide is evolved and the following compounds are formed (in parentheses are given the yields in mole %): (III) (21); (I; R = Me) (~21); (I; R = *cyclo*hexyl) (~12); (II; R = Me) (~22); (II; R = *cyclo*hexyl) (~7). The formation of (II; R = Me or *cyclo*hexyl) is in agreement with Fry and Kendall's mechanism (*J.*, 1951, 1716) involving initial quaternisation of the nitrogen atom in (I) by the alkyl halide. On the other hand, the formation of (III) and (I; R = *cyclo*hexyl) in substantial amounts cannot be satisfactorily explained on this basis and it must be concluded that decomposition of an initially formed sulphonium salt is also operative (Davies and Sexton, *J.*, 1942, 304; Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502):



(*B*) *2-Alkenylthiobenzothiazoles.* The reversible thermal isomerisations of (I) and (II) (R = alkenyl) are analogous to the Claisen rearrangement of alkenyl aryl ethers to

o-alkenylphenols and related rearrangements (see Tarbell, *Chem. Reviews*, 1940, **27**, 495; "Organic Reactions," Wiley, New York, 1944, Vol. II, p. 5).

Two unimolecular mechanisms are considered possible for the reversible isomerisations at present under discussion, *viz.*: (1) an intramolecular process involving a cyclic transition complex; and (2) an ionic process involving the formation of the mesomeric thiobenzothiazolyl and alkenyl ions:



Efforts to obtain evidence favouring one or other of these mechanisms were made for (I) and (II) (R = allyl and *cyclo*hex-2-enyl). In Table 4 are given the values for the Arrhenius energy of activation (*E*), the temperature-independent (*PZ*) factor, and the entropy of activation ($\Delta S^{\ddagger}$) for the isomerisation of the above compounds and for the decomposition of (I; R = *cyclo*hexyl). The $\Delta S^{\ddagger}$ values were derived from Eyring's equation for unimolecular gas-phase reactions (Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," McGraw-Hill, New York, 1941, p. 295), a value of unity being assumed for the transmission coefficient κ (cf. Shuler and Murphy, *J. Amer. Chem. Soc.*, 1950, **72**, 3155):

TABLE 4.

Reactant	*E* (kcal. mole^{-1})	*PZ* (sec.$^{-1}$)	$\Delta S^{\ddagger}$ (cal. deg.$^{-1}$ mole^{-1}) at 140° c
(I; R = allyl) †	31·3	$9{\cdot}6 \times 10^{10}$	−10·9
(II; R = allyl) †	34·6	$3{\cdot}9 \times 10^{11}$	−8·1
(I; R = *cyclo*hex-2-enyl) †	29·0	$2{\cdot}2 \times 10^{11}$	−9·2
(II; R = *cyclo*hex-2-enyl) †	33·5	$1{\cdot}8 \times 10^{13}$	−0·5
(I; R = *cyclo*hexyl) *	43·5	$6{\cdot}2 \times 10^{13}$	+1·9

* Data from $k_{uni.}$ at 200°. † Data from $k_{uni.}$ at 140°.

The large negative entropies of activation for the isomerisations of (I; R = allyl and *cyclo*hex-2-enyl) and (II; R = allyl) are consistent with the intramolecular mechanism (1). Similar interpretations have been given for the large negative entropies of activation observed for unimolecular Claisen rearrangements (Kincaid and Tarbell, *J. Amer. Chem. Soc.*, 1939, **61**, 3085; Murphy and Stein, *ibid.*, 1952, **74**, 1041; Shuler and Murphy, *loc. cit.*). For (II; R = *cyclo*hex-2-enyl) the *PZ* factor is normal and there is only a small negative entropy of activation; the significance of this result is obscure.

It could be argued that the rate-determining unimolecular heterolytic fission process (mechanism 2) may also be attended by a low *PZ* factor and thus a large negative entropy of activation, since the formation of the transition state may be accompanied by an increase of solvation. Such is the case for the Menschutkin reaction (Bell, *J.*, 1943, 629). However, in the decomposition of (I; R = *cyclo*hexyl) where the rate-determining step is undoubtedly a heterolytic fission of the C–S bond as required by mechanism (2), a normal *PZ* factor and a small positive entropy of activation are observed. It appears, therefore, that this dissociation does not involve any pronounced solvation of the ionic transition complex by the reactant or product molecules, and thus it may be inferred that the low *PZ* factors and large negative entropies of activation for the allyl-group isomerisations denote that mechanism (1) is operative.

The change in the reaction course of (I) and (II) (R = *cyclo*hex-2-enyl) when the temperature is increased from 140° to 200° is in keeping with intrusion of mechanism (2) at the higher temperature. Analogous decompositions, as alternatives to the normal rearrangement, have been observed with certain alkenyl aryl ethers (Tarbell, *locc. cit.*; Alexander and Kluiber, *J. Amer. Chem. Soc.*, 1951, **73**, 4304).

Further attempts to define the mechanism of the isomerisation of (I) and (II) (R = allyl and *cyclo*hex-2-enyl) were made by investigating the reaction of (I; R = *trans*-but-2-enyl). The isomerisation at 200° unexpectedly proved to be considerably slower than that of (I; R = allyl). Analysis of the non-equilibrated product after 20 hours at 200° indicated, directly or indirectly, the presence of the isomers listed in Table 5. The results suggest

TABLE 5. *Isomerisation of* (I; R = trans-*but*-2-*enyl*); 200° ± 1°; 20·0 *hours.*

R =	*trans*-But-2-enyl	*cis*-But-2-enyl	1-Methylallyl
(I), % of total	~85	~15	~0
(II), % of total	(major) ~80—84	(minor)	~16—20

that both mechanisms (1) and (2) are operative in this case. Examination of models of the relevant molecules reveals that the formation of the cyclic transition state from (I; R = *trans*-but-2-enyl) necessary for the occurrence of (1) results in considerable steric interference between the terminal methyl group and the benzene ring. The intervention of mechanism (2) is thus favoured, with the formation of all three isomers of (II; R = but-2-enyl and 1-methylallyl)—the *trans*-but-2-enyl isomer being predominant in agreement with data from S_N1 substitutions and rearrangements in which the mesomeric methylallyl carbonium ion is an intermediate (Alexander, "Principles of Ionic Organic Reactions," Wiley, New York, 1950, Chapter 15; Catchpole and Hughes, *J.*, 1948, 4). No steric interference of the type considered above occurs with the other isomers or with (I) and (II) (R = allyl and *cyclo*hex-2-enyl) and therefore these may isomerise intramolecularly. The appearance of (II; R = 1-methylallyl) and the apparent absence of (I; R = 1-methylallyl) is understandable on the basis of the above reaction tendencies coupled with the expected higher velocity constant for the rearrangement of the latter isomer, as deduced from the analogous isomerisation of (I) and (II) (R = allyl). The slight intrusion of the decomposition reaction (ii), yielding (III) (see Table 1), is a consequence of the methylallyl carbonium ion being an intermediary in the reaction. The slowness of the isomerisations in this case, as compared with that of (I) and (II) (R = allyl), may be due to the higher *E* required for the operation of the ionic process. The *reduced* facility of isomerisation on passing from R = allyl to R = *trans*-but-2-enyl appears inexplicable in terms of a common reaction mechanism and hence lends support to the duality of mechanisms now proposed (Braude and Jones, *J.*, 1946, 122, 128; Tarbell and Wilson, *J. Amer. Chem. Soc.*, 1942, **64**, 607). The mechanism operating in the isomerisations of (I) and (II) (R = alkenyl) is seen to be critically dependent on the configurational nature of the alkenyl group. Similar effects have been observed in the thermal isomerisations of alkenyl thiocyanates (Mumm and Richter, *Ber.*, 1940, **73**, 843; Bergmann, *J.*, 1935, 1361).

The ionic processes discussed above afford reasonable and self-consistent explanations of the varying characteristics of the isomerisations and decompositions of the molecular types (I) and (II). Direct evidence to refute the suggestion that free-radical intermediates might be involved (Fry and Kendall, *J.*, 1951, 1723) is obtained from experiments concerned with the behaviour of benzyl-type radicals under the decomposition conditions. On heating di(benzothiazol-2-yl) disulphide with dibenzyl at 200° or 230° a dehydrogenating reaction ensues which gives approximately 90% of the thiol (III), *trans*-stilbene, and a large amount of a dehydropolymer of dibenzyl. It follows from Part I that the dehydrogenating unit is the thiobenzothiazolyl radical, and therefore that the dehydropolymer represents a major molecular product of the *radical* $C_6H_5\cdot\dot{C}H\cdot CH_2\cdot C_6H_5$. This substance and dibenzyl were not detected in the decomposition of (I; R = benzyl), the liberated benzyl fragments appearing entirely as *trans*-stilbene (p. 4238). Again, when (I; R = *cyclo*hexyl) was heated in dibenzyl at 230°, (III) and *cyclo*hexene were the sole products. If *cyclo*hexyl and thiobenzothiazolyl radicals were intermediates, not only would radical attack on dibenzyl be expected to yield *trans*-stilbene and the dehydropolymer, but coupling of the *cyclo*hexyl radicals should also be evident (cf. Farmer and Moore, *J.*, 1951, 131).

Experimental

Ultra-violet light absorption measurements were made with absolute ethanol solutions by means of a Hilger Uvispek photoelectric spectrophotometer. Infra-red spectra were recorded by means of a Grubb-Parsons single-beam spectrometer.

Preparation of Materials.—*2-Methylthiobenzothiazole* (I; R = Me) had m. p. 49·5° (Found: C, 53·1; H, 4·0; N, 7·75; S, 35·2. Calc. for $C_8H_7NS_2$: C, 53·0; H, 3·9; N, 7·7; S, 35·35%). Light absorption: max., 2780, 2880, 2990 Å; ε, 12,800, 11,100, 8400 respectively].

3-Methyl-2-thiobenzothiazoline (II; R = Me) was prepared by the iodine-catalysed isomerisation of (I; R = Me) at 210—215° for 3 hours (Reed *et al.*, *loc. cit.*). It crystallised from ethanol in colourless prisms, m. p. 89·0—90·5° (Found: C, 53·05; H, 4·0; N, 7·65; S, 34·9%). Light absorption: max., 2300, 2410, 3240 Å; ε, 15,000, 15,600, 28,300 respectively.

2-iso*Propylthiobenzothiazole* (I; R = Pr^i) was prepared from the sodium derivative of 2-mercaptobenzothiazole and *iso*propyl bromide in refluxing ethanol (yield, 54·6%), b. p. 105—108°/<0·01 mm., n_D^{20} 1·6358 (Found: C, 57·4; H, 5·45; N, 6·75; S, 30·55. $C_{10}H_{11}NS_2$ requires C, 57·4; H, 5·3; N, 6·7; S, 30·6%). Light absorption: max., 2820, 2900, 3000 Å; $E^{1\%}_{1\,cm.}$, 585, 547, 456 respectively. Alkali-titration indicated the presence of *ca.* 0·4% of (III); $E^{1\%}_{1\,cm.\ 3265}$ 12·8 indicated 0·45% of (II; R = Pr^i).

2-n-*Octylthiobenzothiazole* (I; R = *n*-C_8H_{17}), prepared as for (I; R = Pr^i), had b. p. 151—155°/<0·01mm., n_D^{20} 1·5873 (yield, 71·3%) (Found: C, 64·25; H, 7·75; N, 5·2; S, 23·0. $C_{15}H_{21}NS_2$ requires C, 64·5; H, 7·6; N, 5·0; S, 22·9%). Light absorption: max., 2815, 2900, 3010 Å; $E^{1\%}_{1\,cm.}$, 475, 434, 353 respectively. Alkali-titration indicated 0·4% of (III), and $E^{1\%}_{1\,cm.\ 3265}$, 6·5 indicated the absence of (II; R = *n*-C_8H_{17}).

2-*cyclo*Hexylthiobenzothiazole (I; R = *cyclo*hexyl), prepared as for (I; R = Pr^i), crystallised from aqueous ethanol in needles, m. p. 47—48° (39%) (Found: C, 62·6; H, 6·1; N, 5·65, 5·8; S, 25·5. Calc. for $C_{13}H_{15}NS_2$: C, 62·6; H, 6·1; N, 5·6; S, 25·7%). Light absorption: max., 2810, 2890, 3000 Å; ε, 13,000, 12,200, 10,300, respectively. Ultra-violet analysis and alkali-titration showed the absence of (III) and (II; R = *cyclo*hexyl).

2-Benzylthiobenzothiazole (I; R = CH_2Ph), prepared as for (I; R = Pr^i) (yield, 99%), crystallised from aqueous ethanol in colourless prismatic plates, m. p. 39·5—40·5° (72%) (Found: C, 65·4; H, 4·5; N, 5·6, 5·75; S, 24·6. Calc. for $C_{14}H_{11}NS_2$: C, 65·35; H, 4·3; N, 5·45; S, 24·9%). Light absorption: max., 2810, 2890, 3000 Å; ε, 13,500, 12,700, 10,500 respectively. Ultra-violet analysis and alkali-titration showed the absence of (III) and (II; R = CH_2Ph).

2-*Allylthiobenzothiazole* (I; R = C_3H_5).—Allyl bromide (66·5 g., 0·55 mol.; b. p. 69·5—70°/750 mm., n_D^{20} 1·4695) was added to a stirred suspension of the sodium derivative of 2-mercaptobenzothiazole (III) (83·6 g., 0·5 mol.; NaOMe, 27 g., 0·5 mol.) in toluene, the mixture being heated at 80—90° for 7 hours. The product was poured into water, and the toluene layer separated and washed with 10% aqueous sodium hydroxide (2 × 150 ml.), followed by water, and finally dried ($CaCl_2$). Removal of solvent and distillation of the product gave the *thiazole* (I; R = C_3H_5), b. p. 126—129°/0·05 mm., n_D^{20} 1·6627 (71·4%) (Found: C, 58·0; H, 4·35; N, 6·95; S, 31·05. $C_{10}H_9NS_2$ requires C, 57·9; H, 4·4; N, 6·75; S, 30·95%). Light absorption: max., 2800, 2880, 3000 Å; $E^{1\%}_{1\,cm.}$, 609, 555, 444, respectively. The infra-red spectrum shows bands at 1636 and 920 cm.$^{-1}$, characteristic of the R·CH=CH_2 grouping. The vibration at ~990 cm.$^{-1}$, also characteristic of this grouping, is masked by a strong skeletal vibration. Alkali-titration showed the absence of (III) and $E^{1\%}_{1\,cm.\ 3265}$, 10·6 indicated 0·65% of (II; R = C_3H_5).

2-(trans-*But*-2-*enylthio*)*benzothiazole* (I; R = *trans*-CH_3·CH:CH·CH_2).—*trans*-But-2-en-1-ol, prepared by the reduction of *trans*-crotonaldehyde (b. p. 101·1—101·2°/742 mm., n_D^{20} 1·4370) with lithium aluminium hydride (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197), had b. p. 120·9—121·2°/759 mm., n_D^{25} 1·4266. The infra-red spectrum showed that the R·CH:CH_2 grouping was absent. *trans*-But-2-enyl chloride was prepared from the alcohol by Hatch and Nesbitt's method (*ibid.*, 1950, **72**, 727), and had b. p. 83·9—84·1°/759 mm., n_D^{20} 1·4353, n_D^{25} 1·4329. Infra-red analysis showed the presence of *ca.* 1% of 1-methylallyl chloride. The chloride (47·3 g., 0·523 mol.) was caused to react with the sodium derivative of (III) (83·6 g., 0·50 mol.; NaOMe, 27·0 g., 0·50 mol.) in ethanol (100 ml.) during 4 hours at 75—80°. The reactant concentrations were those conducive to S_N2 substitution (salt, ~2·9M; chloride, ~3·0M) (cf. Catchpole and Hughes, *J.*, 1948, 4). The crude product (98·8 g., 89%), on distillation, gave the pure *butenyl* compound (89·2 g., 81%), b. p. 110—115°/0·01—0·02 mm., which crystallised from aqueous ethanol in long colourless prisms, m. p. 42·0—42·5° (Found: C, 59·75; H, 4·95; N, 6·5; S, 28·8. $C_{11}H_{11}NS_2$ requires C, 59·7; H, 5·0; N, 6·3; S, 29·0%). Light

absorption: max., 2810, 2890, 3000 Å; ε, 13,200, 12,300, 10,100, respectively. Alkali-titration showed the absence of (III) and ultra-violet analysis ($E^{1\%}_{1\ cm.\ 3265}$, 3·0) indicated the absence of (II; R = CH_3·CH:CH·CH_2). The infra-red spectrum shows bands at 1667 and 961 cm.$^{-1}$ attributable to *trans*-R·CH:CH·R. Skeletal vibrations at 992 and 927 cm.$^{-1}$ (see below) will mask weak bands due to (I; R = 1-methylallyl); however, the absence of a band at ~1640 cm.$^{-1}$ indicates that this isomer is probably absent.

Mixture of 2-(trans-*But*-2-*enylthio*)*benzothiazole and* 2-(1-*Methylallylthio*)*benzothiazole*.—These were prepared as described for (I; R = *trans*-but-2-enyl) when a mixture of *trans*-but-2-enyl chloride and 1-methylallyl chloride (b. p. 64·0—83·9°/759 mm., n_D^{20} 1·4263 containing ~36% of the latter isomer, as based on the band at ~925 cm.$^{-1}$) was used. The mixed sulphides had b. p. 107—111°/0·005 mm. (Found: C, 59·65; H, 5·05; N, 6·4%). Light absorption: max., 2815, 2900, 3010 Å; $E^{1\%}_{1\ cm.\ 2815}$, 592 and $E^{1\%}_{1\ cm.\ 3265}$, 13·5, indicating 99·0% of (I) and 1·1% of (II). The infra-red spectrum was identical with that of pure (I; R = *trans*-CH_3·CH:CH·CH_2) except that a band occurred at 1636 cm.$^{-1}$, due to the R·CH:CH_2 grouping, absent in the latter. The similarity of the spectra of the mixture and pure (I; R = *trans*-CH_3·CH:CH·CH_2) in the 10-μ region suggests that both bands (at ~910, 990 cm.$^{-1}$) due to the C–H deformation of the R·CH:CH_2 grouping are masked by skeletal vibrations.

2-(cyclo*Hex*-2-*enylthio*)*benzothiazole* (I).—The preparation of this compound and its isomer (II) is described in Part I.

2-*Mercaptobenzothiazole* (III).—A pure sample, kindly supplied by Dr. D. S. P. Roebuck of Monsanto Chemicals Ltd. (Ruabon), had m. p. 178—179° (Found: C, 50·0; H, 3·15; N, 8·45; S, 38·2%; equiv., 166·1, 165·1. Calc. for $C_7H_5NS_2$: C, 50·3; H, 3·0; N, 8·4; S, 38·3%; equiv., 167·2). Light absorption: max., 3200 Å; ε, 23,400. Koch (*J.*, 1949, 401) gives max., 3250 Å and ε, 27,500, and Morton and Stubbs (*J.*, 1939, 1321) gives max., 3250 Å, ε, 27,000. The value of 3200 Å, obtained by photoelectric spectrometry, was checked with another sample of (III). The photographic method gave, for the above sample, max., 3210 Å, ε, 24,000, so that it must be concluded that the results of Morton and Stubbs (*loc. cit.*) and Koch (*loc. cit.*) are in error.

Thermal isomerisations and decompositions.

General Analytical Procedure.—Weighed samples of the compounds were heated *in vacuo* in a thermostatically controlled oil-bath for the appropriate time. Estimation of (III) was made by titration of an ethanolic solution of the product with standard sodium hydroxide (phenolphthalein) or by the alkali-extraction procedure described in Part I. Isomerisations of (I) and (II) were followed by measuring the change in the ultra-violet light absorption properties. (I) exhibits intense absorption in the region 2800—3000 Å, which is resolved into three maxima at about 2810, 2890, and 3000 Å (the exact positions depending on the nature of R), and has negligible absorption in the region of 3250 Å (cf. Morton and Stubbs, *loc. cit.*). (II) has maxima at about 2400 and 3260 Å and a minimum at about 2800 Å (Morton and Stubbs, *loc. cit.*). (II) was thus estimated by measuring the intensity of absorption at 3265 Å, allowance being made for the absorption of (III) (if present) which also exhibits high-intensity absorption at this wave-length. The concentration of (I) was obtained by difference and checked by measuring the absorption intensity of the mixture at 2815 Å. The absorption intensities for pure (I), (II), and (III) at 2815 and 3265 Å are recorded in Table 6.

TABLE 6. *Ultra-violet spectroscopic data for* (I) *and* (II) *(in ethanol).*

	(I)		(II)	
R	$E^{1\%}_{1\ cm.\ 2815}$	$E^{1\%}_{1\ cm.\ 3265}$	$E^{1\%}_{1\ cm.\ 2815}$	$E^{1\%}_{1\ cm.\ 3265}$
Methyl	693	2·2	147·9	1505
*iso*Propyl	590	~2	105·0 *	1250 *
n-Octyl	476	~2	78·0 *	931 *
*cyclo*Hexyl	522	2·0	86·0	1046
*cyclo*Hex-2-enyl	548·3	~2	88·8	1058
Benzyl	526	4·3	81·6	1000
Allyl	610	~2	108·5	1317
trans-But-2-enyl	597	3·0	104·1	1218
Hydrogen (III)	—	—	170·5	1238

* Based on values for (II; R = *cyclo*hex-2-enyl).

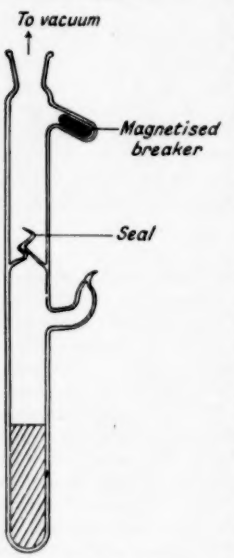
Thermal Isomerisations and Decompositions.—(1) The sulphide (I; R = Me), when heated at 200° ± 2° for 48·0 hours, gave a product containing unchanged (I; R = Me) (98%), (II; R = Me) (2·0%), and (III) (0·13%) (Light absorption: $E^{1\%}_{1\ cm.\ 2815}$, 682; $E^{1\%}_{1\ cm.\ 3265}$, 31·1).

(2) The sulphide (I; R = Pr^{i}) (3·73 g.), heated at 200° ± 2° for 48·0 hours, gave (III) (0·386 g., 0·130 mol.) and an alkali-insoluble product (3·19 g.), n_D^{20} 1·6371, consisting of (I; R = Pr^{i}) (97·5%) and (II; R = Pr^{i}) (2·5%) (Found: C, 57·4; H, 5·3; N, 6·7%. Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 575·7; $E^{1\%}_{1\text{ cm. }3265}$, 34·1).

(3) The sulphide (I; R = *n*-C_8H_{17}) (8·57 g.), on being heated at 200° ± 1° for 48·0 hours, gave (III) (0·085 g.) and an alkali-insoluble product (8·35 g.) consisting of (I) (99%) and (II) (R = *n*-C_8H_{17}) (~0·9%) (Found: C, 64·4; H, 7·6; N, 4·9; S, 22·7, 22·85%. Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 472·3; $E^{1\%}_{1\text{ cm. }3265}$, 10·0). A second sample of the sulphide, heated as above, but from which (III) had not been removed, contained ~0·9% of the latter (Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 472·9; $E^{1\%}_{1\text{ cm. }3265}$, 21·0).

(4) (I; R = *cyclo*Hexyl). (*a*) The sulphide (5·94 g.) was heated at 200° ± 2° for 72·4 hours in the apparatus shown in Fig. 2. This was connected to a weighed receiver, the assembly was evacuated and isolated from the line, and after breakage of the seal the volatile products were transferred to the receiver by cooling of the latter in liquid air. A second evaporative distillation of the volatile product (0·195 g.) gave almost pure *cyclo*hexene (0·192 g.), n_D^{20} 1·4473 (Found: C, 87·2; H, 12·2; S, 0·3. Calc. for C_6H_{10}: C, 87·7; H, 12·3%). The infra-red spectrum of this sample was identical with that of pure *cyclo*hexene. The non-volatile product consisted of (III) (0·443 g., 0·111 mol.), m. p. 176—178°, mixed m. p. 178—179°, which after crystallisation from water had m. p. and mixed m. p. 178—179°, and an alkali-insoluble product (5·21 g.), m. p. and mixed m. p. with (I; R = *cyclo*hexyl) 45—48°, containing (I) (98·9%) and (II; R = *cyclo*hexyl) (0·25%) (Found: C, 62·8; H, 6·0; N, 5·8%. Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 515·7; $E^{1\%}_{1\text{ cm. }3265}$, 4·5).

FIG. 2.



(*b*) The sulphide (4·956 g.), when heated at 200° ± 2° for 48·0 hours and worked up in the usual way, gave (III) (0·255 g., 0·077 mol.) and unchanged sulphide (4·48 g.), m. p. and mixed m. p. 46·5°.

(*c*) Heating the sulphide (6·110 g.) at 230° ± 1° for 5·0 hours and working up the product as in (*a*) gave: (i) slightly impure *cyclo*hexene [0·217 g., 92·5% based on yield of (III)], n_D^{20} 1·4477 (Found: C, 87·1; H, 12·1; S, 0·5%), the infra-red spectrum of which was identical with that of pure *cyclo*hexene; (ii) (III) (0·478 g., 0·117 mol.); and (iii) a mixture of (I) (~100%) and (II; R = *cyclo*hexyl) (~0·15%) (Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 527; $E^{1\%}_{1\text{ cm. }3265}$, 3·6).

(*d*) *Iodine-catalysed decomposition.* The sulphide (3·038 g.) and iodine (46·3 mg., equiv. to 15·24 mg. per g. of sulphide) were heated at 200° ± 1° for 6·0 hours in the apparatus shown in Fig. 2. The products consisted of: (i) slightly impure *cyclo*hexene (0·180 g.), b. p. 82·5°, n_D^{20} 1·4500 (Found: C, 86·1; H, 11·8%), identified by its infra-red spectrum; (ii) (III) (0·613 g., 0·302 mol.), m. p. and mixed m. p. 178—179° (Found: equiv., 167·5. Calc. for $C_7H_5NS_2$: equiv., 167·2); (iii) unchanged sulphide (1·90 g.), m. p. 43—46°, which after crystallisation from aqueous ethanol had m. p. and mixed m. p. 47—48°; and (iv) 3-cyclo*hexyl*-2-*thiobenzothiazoline* (II; R = *cyclo*hexyl) (0·14 g.), m. p. 97—100°, which was separated from (iii) by virtue of its insolubility in concentrated hydrochloric acid (cf. Reed *et al.*, *loc. cit.*). On crystallisation from ethanol pure (II; R = *cyclo*hexyl) was obtained as light yellow prismatic needles, m. p. 104—105° (Found: C, 62·6; H, 6·2; N, 5·55; S, 25·4. $C_{13}H_{15}NS_2$ requires C, 62·6; H, 6·1; N, 5·6; S, 25·7%). Light absorption: max., 2420, 3280 Å; ε, 13,700, 26,000, respectively).

(*e*) In an experiment similar to (*d*) the sulphide (3·004 g.), heated with iodine (44·7 mg., 14·9 mg. per g. of sulphide) at 200° ± 1° for 18·1 hours, gave: (i) impure *cyclo*hexene (0·223 g.), n_D^{23} 1·4516; (ii) (III) (0·597 g., 0·296 mol.); (iii) unchanged sulphide (1·60 g.); and (iv) (II; R = *cyclo*hexyl) (0·4 g.), m. p. 103—105°.

(*f*) *Decomposition in dibenzyl solution.* Heating a mixture of the sulphide (3·00 g.) and dibenzyl (3·00 g.) at 230° ± 1° for 8·0 hours gave (III) (0·369 g., 0·183 mol.) and an alkali-insoluble product which was separated, by trituration with concentrated hydrochloric acid, into the unchanged sulphide (2·38 g.), m. p. and mixed m. p. 46—47°, and dibenzyl (2·95 g.) containing ~0·5% of *trans*-stilbene (Light absorption: max., 2540, 2590, 2650, 2690, 2950 Å; $E^{1\%}_{1\text{ cm. }2590}$, 26·16; $E^{1\%}_{1\text{ cm. }2950}$, 7·64). The original dibenzyl contained ~0·4% of *trans*-stilbene (Light absorption: max., 2540, 2590, 2650, 2690 Å; $E^{1\%}_{1\text{ cm. }2590}$, 26·14; $E^{1\%}_{1\text{ cm. }2950}$, 6·04].

(5) The sulphide (I; R = CH_2Ph) (4·017 g.), after 48·0 hours at 200° ± 2°, gave (III) (0·525 g., 0·201 mol.) and an alkali-insoluble product (3·30 g.). The latter partly dissolved in warm light petroleum (b. p. 40—60°), leaving (II; R = CH_2Ph) (0·14 g.) which crystallised from ethanol in light yellow needles, m. p. 150·0—150·5° (Reed *et al.*, *loc. cit.*, give m. p. 149—150°) (Found: C, 65·35; H, 4·6; N, 5·4; S, 24·5%). Light absorption: max., 2410, 3260 Å; ε, 12,900, 25,800 respectively. Chromatographic separation of the petroleum solution (200 ml.) on alumina (90 g.) by elution with successive 100-ml. portions of benzene–light petroleum (1 : 1 by vol.) gave: (i) a light yellow solid (0·85 g.); (ii) unchanged (I; R = CH_2Ph) (1·58 g.), m. p. 39—40·5°, mixed m. p. 40—41°; and (iii) slightly impure (ii) (0·30 g.), m. p. 37—39°, mixed m. p. 38—41°. Fraction (i), in light petroleum (b. p. 40—60°) (100 ml.), was rechromatographed on alumina (20 g.) and developed with the same solvent to give the following fractions (volumes in parentheses refer to eluate): (*ia*) (135 ml.), slightly impure *trans*-stilbene (0·10 g.), m. p. 112—123, which on crystallisation from aqueous ethanol gave the pure compound (0·06 g.), m. p. and mixed m. p. 124—124·5° (Found: C, 93·1; H, 6·65. Calc. for $C_{14}H_{12}$: C, 93·3; H, 6·7%). Light absorption: max., 2950 Å, ε, 29,800; (*ib*) (25 ml.), impure *trans*-stilbene (0·05 g.) which was added to the mother-liquor from (*ia*) and recrystallised, to give almost pure *trans*-stilbene (0·05 g.), m. p. 121—124·5°, mixed m. p. 122—124·5°; (*ic*) (20 ml.), a mixture of *trans*-stilbene and sulphide (0·03 g.); and (*id*) (column stripped with benzene), unchanged (I; R = CH_2Ph) (0·50 g.), m. p. and mixed m. p., 39—40°.

(6) (*a*) The sulphide (I; R = allyl) (14·72 g.) was heated at 200° ± 1° for 3·0 hours. Alkali-extraction of the product in chloroform showed the absence of (III). Trituration of the alkali-insoluble product (13·98 g.) with concentrated hydrochloric acid gave the *thiazoline* (II; R = allyl) (12·39 g.), m. p. 65—67°, which crystallised from aqueous ethanol (charcoal) in colourless plates, m. p. 67·5—68·5° (Found: C, 57·85; H, 4·45; N, 6·7; S, 30·6. $C_{10}H_9NS_2$ requires C, 57·9; H, 4·4; N, 6·75; S, 30·95%). Light absorption: max., 2400, 3240 Å; ε, 13,840, 27,360 respectively. The infra-red spectrum shows bands at 1641 and 924 cm.$^{-1}$ attributable to the R·CH:CH_2 grouping.

(*b*) By heating the sulphide (4·67 g.) at 200° ± 2° for 48·0 hours in the apparatus described in Fig. 2 it was shown that no volatile products were formed and that (III) was again absent. The product (4·48 g.) gave (II; R = allyl) (3·94 g.), m. p. 67·0—67·5°, on trituration with concentrated hydrochloric acid.

(7) (*a*) The sulphide (I; R = *trans*-but-2-enyl) (10·02 g.), heated at 200° ± 1° for 20·0 hours, gave (III) (0·147 g., 0·0194 mol.), m. p. and mixed m. p. 177—179°, and an alkali-insoluble product (9·85 g.) separable by trituration with concentrated hydrochloric acid into (i) an insoluble product (2·87 g.), m. p. 62—73°, and (ii) a soluble product (5·98 g.) regenerated by neutralisation of the acid. (i) consisted of (II; R = *x*-methylallyl) (96·5%) (Found: C, 59·9; H, 5·2; N, 6·35; S, 28·7%). Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 103·6; $E^{1\%}_{1\text{ cm. }3265}$, 1174. The infra-red spectrum shows bands at 965 cm.$^{-1}$, due to *trans*-CHR:CHR, and at 1635 and 924 cm.$^{-1}$, due to R·CH:CH_2. The intensities of the bands at 1635 and 924 cm.$^{-1}$ indicate the presence of 16—20% of (II; R = 1-methylallyl). Crystallisation of (i) from aqueous ethanol gave an apparently pure sample of the *thiazoline* (II; R = *trans*-but-2-enyl) as colourless needles, m. p. 77·5—78·5° (Found: C, 59·5; H, 5·0; N, 6·25; S, 28·65, 29·0%). Light absorption: max., 2410, 3260 Å; ε, 15,000, 27,300 respectively. The infra-red spectrum of this compound shows a strong band at 965 cm.$^{-1}$ indicating the *trans*-CHR:CHR grouping; the absence of a band at 1635 cm.$^{-1}$ suggests the absence of (II; R = 1-methylallyl). (ii), a partly crystallising light-orange oil, was a mixture of (I; R = *x*-methylallyl) (91·4%) and (II; R = *x*-methylallyl) (3·9%) (Found: C, 59·45; H, 5·15; N, 6·35, 6·4%). Light absorption: max., 2810, 2890, 3000 Å; $E^{1\%}_{1\text{ cm. }2815}$, 549·5; $E^{1\%}_{1\text{ cm. }3265}$, 47·4. The infra-red spectrum of (ii) is similar to, but not identical with, that for pure (I; R = *trans*-but-2-enyl). Since the latter compound has a skeletal vibration at 927 cm.$^{-1}$ the presence of a band in this position cannot be used as diagnostic evidence for (I; R = 1-methylallyl). However, the absence of a band at ~1640 cm.$^{-1}$ strongly suggests the absence of this compound. Absorption in the region of 670 cm.$^{-1}$ is only slightly greater than that for pure (I; R = *trans*-but-2-enyl), making it difficult to establish the presence of the *cis*-CHR:CHR′ grouping (however, see below). The intensity of the 965 cm.$^{-1}$ band shows that ~85% of (I; R = *trans*-but-2-enyl) is present.

Distillation of a portion (4·45 g.) of (ii) gave (ii*a*), b. p. 118—120°/0·04 mm. (3·80 g.), containing (I) (96·5%) and (II; R = *x*-methylallyl) (~1·7%) (Found: C, 59·6; H, 5·0; N, 6·4; S, 28·6%. Light absorption: max., 2815, 2900, 3010 Å; $E^{1\%}_{1\text{ cm. }2815}$, 578; $E^{1\%}_{1\text{ cm. }3265}$, 21·4). The infra-red spectrum of this sample is very similar to that of (ii), except that the band intensity at 1674 cm.$^{-1}$ in the latter is greatly reduced and the band centre now appears at 1667 cm.$^{-1}$

(region for *cis*- and *trans*-CHR:CHR); there is no band in the 1640 cm.$^{-1}$ region. (iia) partly crystallised and filtration of a portion (2·65 g.) gave pure (I; R = *trans*-but-2-enyl) (0·85 g.), m. p. and mixed m. p., 42·0—42·5°. The filtrate (1·66 g.) contained (I) (96·6%) and (II; R = *x*-methylallyl) (2·4%) (Light absorption: max., 2820, 2900, 3010 Å; $E^{1\%}_{1\text{ cm. }2815}$, 579; $E^{1\%}_{1\text{ cm. }3265}$, 29·1). The infra-red spectrum of the filtrate is very similar to that of (ii) and (iia) except that the band at ~1664 cm.$^{-1}$ is intensified slightly. There is no band at ~1640 cm.$^{-1}$ due to the R·CH:CH_2 grouping. Absorption in the region of 670 cm.$^{-1}$, not present in pure (I; R = *trans*-but-2-enyl), may be due to the *cis*-CHR:CHR grouping. The intensity of the band at 965 cm.$^{-1}$ shows that ~60% of *trans*-CHR:CHR is present.

(*b*) Heating the sulphide (10·11 g.) for 48·0 hours at 200° ± 0·5° gave (III) (0·280 g., 0·0367 mol.) and a mixture (9·53 g.) of (I) (33·7%) and (II; R = *x*-methylallyl) (66·5%). Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 270·4; $E^{1\%}_{1\text{ cm. }3265}$, 810.

(8) The thiazoline (II; R = *cyclo*hex-2-enyl) (5·07 g.) was heated at 200° ± 2° for 48·0 hours in the apparatus described in Fig. 2. Evaporative distillation of the product yielded a colourless liquid (0·374 g.), n_D^{20} 1·4795—1·4805 (Found: C, 89·7; H, 9·6; S, 0·45%; C : H = 6 : 7·67). The infra-red spectrum reveals the presence of *cyclo*hexene (~35%), benzene (~65%), and a third component. The ultra-violet spectrum (max., 2430, 2485, 2545, 2605 Å; $E^{1\%}_{1\text{ cm.}}$, 23·5, 32·0, 37·0, 31·8 respectively) confirms the presence of benzene (max., 2430, 2485, 2545, 2605 Å; $E^{1\%}_{1\text{ cm.}}$, 10·5, 19·5, 23·1, 15·6 respectively) and, taken in conjunction with the infra-red spectral data, indicates the presence of a compound having intense absorption in the region of 2400—2700 Å. This is assumed to be *cyclo*hexa-1 : 3-diene (Henri and Pickett, *J. Chem. Phys.*, 1939, **7**, 439, give max., 2475, 2560, 2650 Å; ε, 5400, 7900, 6000 respectively). From the intensities of absorption at 2545 and 2580 Å ($E^{1\%}_{1\text{ cm. }2580}$ 26·3) it is calculated that the mixture contains 2·4% of the diene ($E^{1\%}_{1\text{ cm. }2545,\ 2580}$, 906) and 69% of benzene ($E^{1\%}_{1\text{ cm. }2580}$, 6·6), the light absorption of *cyclo*hexene at these wave-lengths being assumed to be negligible.

Working up the non-volatile product in the usual way gave (III) (1·340 g., 0·391 mol.) and a mixture (3·17 g.) of (I) (27·2%), (II; R = *cyclo*hex-2-enyl) (60·1%), and unidentified polymeric hydrocarbon (~13%) (Found: C, 64·2; H, 5·65; N, 5·5; S, 24·1, 24·4. Calc. for $C_{13}H_{12}NS_2$: C, 63·1; H, 5·3; N, 5·7; S, 25·9%). Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 202·7; $E^{1\%}_{1\text{ cm. }3265}$, 635·6.

(9) The sulphide (I; R = *cyclo*hex-2-enyl) (3·52 g.), heated at 200° ± 2° for 48·0 hours, gave (III) (0·744 g., 0·313 mol.), m. p. and mixed m. p. 178·5°, and a mixture (2·51 g.) of (I) and (II; R = *cyclo*hex-2-enyl) and polymeric hydrocarbon (see Table 11).

Kinetic Data.—The initial rates of decomposition of (I; R = *cyclo*hexyl) were obtained by estimating (III) by the alkalimetric method. The data are summarised in Tables 7 and 8.

TABLE 7. *Decomposition of* (I; R = cyclo*hexyl*).

Temp. (° K)	[I] (mole l.$^{-1}$)	r_i (mole l.$^{-1}$ hr.$^{-1}$)	$10^7 k_{uni.}$ (sec.$^{-1}$)
473° ± 1°	4·24	0·0075	4·9
488° ± 0·5°	4·20	0·032	21
503° ± 1°	4·14	0·115	77
,,	1·89 *	0·052	—
,,	0·90 *	0·024	—
,,	1·83 †	0·047	—

* Diphenyl as diluent. † Dibenzyl as diluent.

TABLE 8. *Decomposition of* (I; R = cyclo*hexyl*) *at* 200° ± 2°.

Time (hours)	12·0	18·0	24·25	36·2	48·0 *	96·0	144·0 †	263·0
Mole % of (III)	2·42	3·38	4·26	6·4	8·3	14·8	19·7	27·3
$10^7 k_{uni.}$ (sec.$^{-1}$)	5·7	5·3	5·0	5·1	5·0	4·6	4·2	3·4

* Product contains (I) (90·7 mole %) and no (II; R = *cyclo*hexyl). Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 496·2; $E^{1\%}_{1\text{ cm. }3265}$, 72·1.

† Product contains (I) (79·1 mole %) and (II; R = *cyclo*hexyl) (0·8 mole %). Light absorption: $E^{1\%}_{1\text{ cm. }2815}$, 465·7; $E^{1\%}_{1\text{ cm. }3265}$, 185·2.

The data for the reversible isomerisations of (I) and (II) (R = allyl, *trans*-but-2-enyl, and *cyclo*hex-2-enyl) and for the combined isomerisation and decomposition of (I) and (II) (R = *cyclo*hex-2-enyl) are summarised in Tables 9—13. The kinetic law for a reversible first-order reaction, $A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$, is given by equation (i):

$$\ln x_e/(x_e - x_t) = (k_1 + k_2)t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (i)$$

where x_t = concentration of A converted into B at time t and x_e = concentration of A converted into B at equilibrium, the initial concentration of B being zero. Thus for the above

TABLE 9. *Reversible isomerisation of* (I) *and* (II) (R = cyclo*hex-2-enyl*) (4·6 *mole l.*$^{-1}$) *at* 140° ± 0·2°.

Time (hrs.)	$E^{1\%}_{1\text{ cm. }2815}$	$E^{1\%}_{1\text{ cm. }3265}$	Mole % of (III)	Mole % of (I)	Mole % of (II)	Total mole %
			(I; R = cyclo*Hex-2-enyl*.)			
0	522·3	61·0	0	94·4	5·6	100·0
0·5	458·5	207·4	—	80·5	19·6	100·1
0·75	434·2	267·9	—	75·1	25·3	100·4
1·0	410·1	327·3	—	69·8	30·9	100·7
1·5	367·3	424·2	—	60·5	40·1	100·6
2·0	336·8	504·8	—	53·7	47·7	101·4
2·5	304·6	566·7	—	46·9	53·6	100·5
3·0	283·4	619·1	—	42·2	58·5	100·7
4·5	239·8	705·5	—	32·9	66·7	99·6
6·0	222·5	750·7	—	29·1	70·9	100·0
12·0	209·5	787·0	0·97	26·0	73·4 *	100·4
24·0	207·2	784·3	1·47	25·6	72·6	99·7
48·0	208·5	782·7	2·25	25·7	71·7	99·7
96·0	211·8	785·2	3·44	26·0	70·7	100·1
			(II; R = cyclo*Hex-2-enyl*.)			
48·0	201·9	801·7	1·22	24·3	74·6	100·1
96·0	202·0	807·0	2·49	24·3	73·7	100·5

* 74·4 mole % on basis of absence of (III).

TABLE 10. *Reversible isomerisation of* (I) *and* (II) (R = cyclo*hex-2-enyl*).

(i) *At* 110·0° ± 0·2°.

Time (hrs.)	0	3·0	6·0	8·0	10·5	13·0	16·0	20·5	24·0	30·0	144·0	192·0
$E^{1\%}_{1\text{ cm. }3265}$	61·0	126·0	179·5	218·6	259·3	299·3	346·6	407·3	449·6	526·4	867·5	867·0
Mole % of (II)	5·6	11·9	17·0	20·7	24·6	28·3	32·8	38·5	42·5	49·8	82·0	82·0

(ii) *At* 125·0° ± 0·2°.

Time (hrs.)	0	1·0	2·0	3·0	4·1	5·0	6·0	8·0	48·0	96·25	144·0
$E^{1\%}_{1\text{ cm. }3265}$	61·0	144·2	223·8	288·6	355·8	405·8	456·8	543·7	822·0	834·2	827·7
Mole % of (II)	5·6	13·6	21·2	27·3	34·0	38·4	43·2	51·4	77·7	78·9	78·3

(iii) *In* cyclo*hexene*; [I] 0·36 *mole l.*$^{-1}$; *at* 140·0° ± 0·2°.

Time (hrs.)	0	1·5	3·0	4·5	6·0	24·0	48·0 *
$E^{1\%}_{1\text{ cm. }3265}$	52·8	209·6	318·1	392·7	448·2	574·0	575·5
Mole % of (II) †	4·8	19·8	30·1	37·1	42·4	54·3	54·4

(iv) *In* cyclo*hexene*; [I] 0·0344 *mole l.*$^{-1}$; *at* 140·0° ± 0·2°.

Time (hrs.)	0	1·5	3·0	4·5	6·0	7·5	24·0	48·0	72·0	96·0
$E^{1\%}_{1\text{ cm. }3265}$	52·8	162·5	262·5	341·7	395·0	437·5	539·2	545·9	550·0	546·9
Mole % of (II) †	4·8	15·4	24·8	32·3	37·3	41·4	51·0	51·6	52·0	51·7

* Estimation of (III) indicates 3·2 mole % of (III) and 51·2 mole % (II).
† Assumed (III) is absent.

TABLE 11. *Thermal isomerisation and decomposition of* (I) *and* (II) (R = cyclo*hex-2-enyl*) *at* 200° ± 1°.

(i) (I; R = cyclo*Hex-2-enyl*).†

Time (hrs.)	1·0	3·0	6·0	10·0	24·0	48·0
$E^{1\%}_{1\text{ cm. }2815}$	288·0	273·0	261·3	244·4	230·1	228·3
$E^{1\%}_{1\text{ cm. }3265}$	648·0	706·5	739·8	763·0	798·3	801·3
Mole % of (III)	13·3	24·7	28·6	29·9	32·4	34·2
Mole % of (I)	39·6	33·7	30·6	27·3	24·0	23·3
Mole % of (II)	48·1	41·9	40·7	41·4	41·9	40·3
Total mole %	101·0	100·3	99·9	98·6	98·3	97·8

(ii) (II; R = cyclo*Hex-2-enyl*).

Time (hrs.)	1·0	3·0	6·0	10·0	24·0	48·0
$E^{1\%}_{1\text{ cm. }2815}$	288·5	264·9	251·1	250·4	233·0	227·0
$E^{1\%}_{1\text{ cm. }3265}$	665·4	750·6	770·2	789·5	800·7	820·6
Mole % of (III)	13·0	24·8	30·5	33·9	33·8	37·3
Mole % of (I)	39·8	31·8	28·1	27·1	24·1	22·3
Mole % of (II)	50·0	45·6	41·5	39·6	40·6	38·9
Total mole %	102·6	102·2	100·1	100·6	98·5	98·5

† Original sample had $E^{1\%}_{1\text{ cm. }2815}$, 522·3; $E^{1\%}_{1\text{ cm. }3265}$, 61·0.

TABLE 12. *Reversible isomerisation of* (I *and* II; R = *allyl*).

(I; R = Allyl):

(i) *At* 140° ± 0·1°; [I] 5·45 mole l.$^{-1}$.

Time (hrs.)	12·0	24·0	36·0	48·1	60·0	72·0	96·0	120·0	144·0	168·0	336·0
$E^{1\%}_{1\text{ cm. }3265}$	131·0	261·5	361·1	464·2	550·3	633·8	744·5	882·5	954·0	1035	1206
Mole % of (II)	10·0	19·9	27·4	35·3	42·1	48·1	56·5	67·0	72·4	78·6	91·6
Time (hrs.)	504·0	672·0									
$E^{1\%}_{1\text{ cm. }3265}$	1223	1229									
Mole % of (II)	92·9	93·3									

(ii) *At* 160° ± 0·1°; [I] 5·4 *mole l.*$^{-1}$.

Time (hrs.)	2·0	4·0	6·0	8·0	12·0	16·0	20·0	24·0	48·0	96·0	144·0
$E^{1\%}_{1\text{ cm. }3265}$	140·3	252·8	359·7	454·1	618·3	749·3	852·6	953·7	1164	1213	1210
Mole % of (II)	10·7	19·2	27·3	34·5	47·0	56·8	64·7	72·4	88·4	92·2	91·9

(iii) *At* 180° ± 0·1°; [I] 5·3 *mole l.*$^{-1}$.

Time (hrs.)	0·5	1·0	1·5	2·0	3·0	4·0	5·0	6·0	16·0	40·0
$E^{1\%}_{1\text{ cm. }3265}$	162·7	296·0	420·8	526·7	700·4	831·2	951·7	1018	1194	1197
Mole % of (II)	12·4	22·5	32·0	40·0	53·2	63·1	72·3	77·3	90·7	90·9

(iv) *At* 200° ± 1°; [I] 5·2 *mole l.*$^{-1}$.

Time (hrs.)	0·25	0·50	0·75	1·05	1·5	2·0	3·0	6·0	48·0 *
$E^{1\%}_{1\text{ cm. }3265}$	302·8	546·8	702·8	887·0	1012	1088	1158	1156	1147
Mole % of (II)	23·0	41·5	53·4	67·4	76·8	82·6	87·9	87·8	87·1

(II; R = *Allyl*):	(v) *At* 160° ± 0·5°.		(vi) *At* 180° ± 0·5°	
Time (hrs.)	96	144	20	40
$E^{1\%}_{1\text{ cm. }3265}$	1220	1224	1199	1193
Mole % of (II)	92·6	92·9	91·1	90·6

* Considerable darkening of product, suggestive of minor side reaction which may explain low result.

TABLE 13. *Reversible isomerisation of* (I; R = trans-*but-2-enyl*) *at* 200° ± 1°.

Time (hrs.)	5·0	20·0	48·0	96·0
$E^{1\%}_{1\text{ cm. }2815}$	497·7	375·2	239·8	193·8
$E^{1\%}_{1\text{ cm. }3265}$	236·8	524·2	830·7	923·0
Mole % of (III)	~0	2·0	3·7	—
Mole % of (I)	80·0	55·2	28·0	—
Mole % of (II)	19·4	41·5	65·3	—

isomerisations obeying equation (i) a linear plot of $\log_{10}[E^{1\%}_{1\text{ cm. }3265e} - E^{1\%}_{1\text{ cm. }3265t}]$ against t, of slope $-0{\cdot}4343(k_1 + k_2)$, should be obtained.

Reaction of cyclo*Hexyl Bromide with* (I; R = Me).—The sulphide (4·53 g., 0·025 mole) and the bromide (4·89 g., 0·03 mole) were heated at 200° ± 1° for 7·0 hours in an oxygen-free atmosphere in an apparatus sealed by mercury traps and connected to a liquid-air trap. A gaseous product, probably methyl bromide, was evolved throughout the reaction period. The main product, on alkali-extraction, gave (III) (0·893 g., 0·21 mol.), m. p. 177·5—178·5°, mixed m. p. 178—179°. Removal of the solvent and unchanged bromide and trituration of the product (3·9 g.) with concentrated hydrochloric acid gave: (i) a mixture (1·7 g.) of (I; R = Me) (~55%) and (I; R = *cyclo*hexyl) (~45%) (Found: C, 58·3; H, 5·15; N, 7·0; S, 29·5. Calc. for above mixture: C, 58·3; H, 5·05; N, 6·55; S, 30·1%); and (ii) a mixture (1·45 g.) of (II; R = Me) (~70%) and (II; R = *cyclo*hexyl) (~30%) [Found: C, 55·55; H, 4·55; N, 7·0; S, 32·25. Calc. for above mixture: C, 55·9; H, 4·5; N, 7·1; S, 32·5%).

Reaction of Di(benzothiazol-2-yl) Disulphide with Dibenzyl.—A mixture of the disulphide and dibenzyl was heated *in vacuo* at 200° ± 0·5° or 230° ± 1° for the appropriate times. The (III) formed was isolated and estimated by alkali-extraction (Part I). *trans*-Stilbene was estimated by ultra-violet spectrometry of the residue, after removal of (III), the absorption intensity being determined at 2950 Å where *trans*-stilbene has a maximum [$E^{1\%}_{1\text{ cm. }2950}$, 1654], and the residue being assumed to consist of *trans*-stilbene and dibenzyl ($E^{1\%}_{1\text{ cm. }2950}$, 6·0). The estimates of *trans*-stilbene so obtained are maximum values since enhanced absorption at 2815 and 3265 Å indicates the presence of other constituents which absorb at 2950 Å.

The disulphide (13·28 g., 0·04 mole) and dibenzyl (7·28 g., 0·04 mole), heated at 200° ± 0·5° for 48·0 hours, gave (III) (11·53 g., 0·069 mole) and a residue (8·69 g.) containing $<$40% of *trans*-stilbene [Found: C, 85·85; H, 6·0; N, 1·60; S, 6·55%; *M* (ebullioscopic, in benzene),

225, 241]. Light absorption: max., 2950 Å; $E^{1\%}_{1\text{ cm. }2950}$, 667·2, $E^{1\%}_{1\text{ cm. }2815}$, 572·0, $E^{1\%}_{1\text{ cm. }3265}$, 283·2. A portion (7·27 g.) of the residue on distillation gave: (i) b. p. 80—110°/0·005 mm. (2·50 g.), containing $\leqslant$25·5% of *trans*-stilbene [Found: C, 90·5, 90·4; H, 7·1, 7·25; N, 0·45; S, 1·1%; *M* (ebullioscopic, in benzene), 161, 182, 183; Light absorption: max., 2950 Å; $E^{1\%}_{1\text{ cm. }2950}$, 424·0, $E^{1\%}_{1\text{ cm. }2815}$, 351·2, $E^{1\%}_{1\text{ cm. }3265}$, 131·6]; (ii) b. p. 110—130°/0·005 mm. (1·52 g.), containing $\leqslant$86% of *trans*-stilbene [Found: C, 90·25; H, 6·6; N, 0·85; S, 2·1%; *M* (ebullioscopic, in benzene), 187, 188, 197; Light absorption: max., 2950 Å; $E^{1\%}_{1\text{ cm. }2950}$, 1424; $E^{1\%}_{1\text{ cm. }2815}$, 1166; $E^{1\%}_{1\text{ cm. }3265}$, 482·3]; and a residue (3·02 g.) containing a dehydropolymer of dibenzyl and 2-mercaptobenzothiazole derivatives [Found: C, 78·95, 78·8; H, 4·85, 4·8; N, 2·5; S, 12·35, 12·5%; *M* (ebullioscopic, in benzene), 314, 348. Light absorption: max., ~3100 Å].

The yields of (III) and the maximum yields of *trans*-stilbene obtained under other reaction conditions are given below.

Reaction of Di(benzothiazol-2-yl) Disulphide with Dibenzyl.

Temp.	Time (hrs.)	Disulphide (10^3 Mole.)	Dibenzyl (10^3 Mole.)	(III) (10^3 Mole.)	Residue (g.)	$E^{1\%}_{1\text{ cm. }2950}$	Max. % of *trans*-stilbene
200° ± 0·5°	24·0	5	5	8·4	—	—	—
230° ± 1°	8·0	5	20	8·8	3·63	241·0	14
,,	24·0	5	20	8·9	3·70	242·5	14
,,	24·0	5	5	9·4	—	—	—

We thank Drs. L. Bateman and G. Gee, F.R.S., for hepful advice and criticism and Messrs. G. Ayrey and D. C. Medcalf for experimental assistance. The microanalyses were conducted under the supervision of Dr. W. T. Chambers. The work described in this and the preceding paper forms part of a programme of fundamental research undertaken by the Board of the British Rubber Producers' Research Association.

British Rubber Producers' Research Association, 48 Tewin Road, Welwyn Garden City, Herts. [*Received, April 25th*, 1952.]

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815. *A Study of Diazo-Compounds by Use of Nitrogen Isotopes. The Reduction of Mixed Diazonium Salts of Anthranilic Acid and Aniline.*

By P. F. Holt and (Mrs.) B. I. Hopson-Hill.

Benzenediazonium chloride is reduced by the cuprammonium ion to yield mainly azobenzene. *o*-Carboxybenzenediazonium chloride yields mainly diphenic acid. When the mixed solutions are reduced the nitrogen of azobenzene-2-carboxylic acid, which is also formed, is derived not from the benzenediazonium but from the carboxybenzenediazonium radical.

Reduction of a diazonium salt may yield, besides nitrogen, one or more of the following products: a diaryl, an azo-compound, an aryl halide, or a phenol. The products formed depend on the nature of the amine and of the reducing agent, and on the conditions.

Vorlander and Meyer (*Annalen*, 1901, **320**, 122) found that the action of ammoniacal cuprous oxide on the diazo-compounds from *m*-xylidine and cumidine gave symmetrical azo-compounds in good yields. Similarly Hodgson, Leigh, and Turner (*J.*, 1942, 744) obtained symmetrical azo-compounds in high yields by the action of freshly precipitated cuprous oxide on acid solutions of naphthalenediazonium sulphates. However, Vorlander and Meyer demonstrated that, when the diazo-compound has chlorine or carboxyl substituents, diaryls are the main product in ammoniacal solution.

The reduction of many different diazotized amines with various reducing agents has been studied extensively by Atkinson, Morgan, Warren, and Manning (*J. Amer. Chem. Soc.*, 1945, **67**, 1513). In particular they examined the products formed when diazotized amines

are reduced with the cuprammonium ion and when mixtures of diazotized amines are reduced, thus synthesizing an unsymmetrical diaryl.

When diazotized *o*- or *p*-nitroaniline is mixed with diazotized anthranilic acid and then reduced with the cuprammonium ion, the products are identical with those obtained by reducing the diazonium salts separately. Reducing a mixture of the diazonium salts of anthranilic acid and aniline, however, gives, not only the expected symmetrical compounds diphenic acid (produced when diazotized anthranilic acid is reduced alone) and azobenzene (produced when diazotized aniline is reduced alone), but also the unsymmetrical azobenzene-2-carboxylic acid (Atkinson, Reynolds, and Murphy, *J. Amer. Chem. Soc.*, 1950, **72**, 1397):

$$C_6H_5{\cdot}N_2^+ + CO_2H{\cdot}C_6H_4{\cdot}N_2^+ \longrightarrow o\text{-}(CO_2H{\cdot}C_6H_4)_2 + C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + CO_2H{\cdot}C_6H_4{\cdot}N{:}N{\cdot}C_6H_5$$

Since the product from diazotized aniline, reduced alone, contains nitrogen and that from diazotized anthranilic acid, reduced alone, does not, it appears likely that the nitrogen atoms present in the azo-group of the azobenzene-2-carboxylic acid are derived from the benzenediazonium ions and that the nitrogen from the diazotized anthranilic acid is eliminated. This part of the reaction mechanism has been studied by isotopically labelling one of the diazonium salts with ^{15}N. Evaluation of the isotope distribution in the reaction products has shown that the nitrogen of the azobenzene-2-carboxylic acid is derived from the diazotized anthranilic acid.

Experimental

^{15}N-Labelled Potassium Nitrite.—Isotopically labelled potassium nitrate (2·8 g.; atom-% ^{15}N 32·4) was fused with potassium hydroxide (0·95 g.) in a crucible. Sodium sulphite (4·5 g.) was added in small portions. A solution of the melt in water was nearly neutralised with hydrochloric acid, and its nitrite content determined colorimetrically (Rider and Mellon, *Ind. Eng. Chem., Anal.*, 1946, **18**, 96). The yield was usually 50—60%. Vaughan, McCane, and Sloane (*J. Amer. Chem. Soc.*, 1951, **73**, 2298) reported yields of 64% by reduction with lead.

Reduction of Diazonium Salts.—Anthranilic acid (0·99 g.), suspended in concentrated hydrochloric acid (1·8 ml.) and water (3 ml.), was diazotized with a solution of potassium nitrite (atom-% ^{15}N 32·4). Aniline (2·03 g.) in water (10 ml.) and hydrochloric acid (7 ml.) was diazotized with unlabelled potassium nitrite (2·5 g. in 20 ml. water). Both diazonium solutions were kept below 5°. Copper sulphate (71·5 g. of $CuSO_4,5H_2O$) was dissolved in water (30 ml.) and concentrated ammonia (12·6 ml.) and cooled to 10°. A solution of hydroxylamine hydrochloride (2·19 g. in 5 ml. of 6N-sodium hydroxide and 7·2 ml. of water) was also cooled to 10° and then added with stirring to the copper sulphate solution.

The diazo-solutions were then mixed and added during 15 minutes to the cuprammonium solution. The crude azobenzene precipitated was filtered off and purified by steam-distillation. It was extracted from the distillate with ether and crystallized (m. p. 67—68°). The ammoniacal distillate was acidified slowly with hydrochloric acid at 90°. At this temperature the azobenzene-2-carboxylic acid collects as a tar but the diphenic acid remains as a supersaturated solution. The azobenzene-2-carboxylic acid, filtered and purified by reprecipitation from a dilute bicarbonate solution, was obtained as an orange solid, m. p. 90—91° (lit., 95° and 92°).

The experiment was repeated, ^{15}N-nitrite being used to diazotize the aniline (0·6 g.), and ^{14}N-nitrite to diazotize the anthranilic acid (0·3 g.).

Measurement of Isotope Ratios.—Nitrogen samples for examination in the mass spectrometer were prepared from the azobenzene and the azobenzene-2-carboxylic acid by the usual procedure (Rittenberg, " Preparation and Measurement of Isotopic Tracers," J. W. Edwards, Ann Arbor, Michigan, 1948, p. 31) except that glucose rather than selenium was used in the Kjeldahl digestion. Test estimations carried out after benzene—→azo-2-naphthol had been subjected to the Rittenberg procedure indicate that the prolonged digestion, which is necessary to ensure the complete removal of volatile substances such as methylamine which interfere with the spectrometric assay, results in the loss of a substantial part of the nitrogen sample when selenium is used (see Table).

Catalyst	Wt. of benzeneazo-2-naphthol (mg.)	Yield of ammonia (% of calc. value)
Selenium	28·4, 33·3	6·9, 6·8
Glucose	28·0, 26·0	70·5, 72·0

Results.—The distribution between the azobenzene and the azobenzene-2-carboxylic acid of the isotopically labelled nitrogen is shown in the annexed Table. The values indicate that the nitrogen of the carboxylic acid is derived from diazotized anthranilic acid.

	^{15}N content of azobenzene (atom-% ^{15}N)	^{15}N content of azobenzene-2-carboxylic acid (atom-% ^{15}N)
Anthranilic acid + $K^{15}NO_2$	0·496	15·4
Aniline + $K^{15}NO_2$	16·4	0·55

^{15}N content of $K^{15}NO_2$ 32·4 atom-%.

Discussion

The formation of symmetrical azo-compounds and symmetrical diaryls by the action of certain reducing agents on aromatic diazo-compounds has been suggested as proceeding with free radicals as intermediates. The mechanism for the action of cuprous hydroxide on acid diazonium sulphate has been described as follows (Hodgson, Leigh, and Turner, *loc. cit.*). The diazonium group accepts an electron from the reducing agent and this either (*a*) causes the elimination of molecular nitrogen, leaving an aryl radical which can combine with another to form a diaryl, or (*b*) causes rearrangement of electrons of the diazonium group, to form a diazo-radical, which can then combine with an aryl radical to form an azo-compound :

$$(a)\ Ph{\cdot}N_2^+ \xrightarrow{e} Ph\cdot + N_2$$
$$Ph\cdot + Ph\cdot \longrightarrow Ph{\cdot}Ph$$

$$(b)\ Ph{\cdot}N_2^+ \xrightarrow{e} Ph{\cdot}N_2\cdot \xrightarrow{Ph\cdot} Ph{\cdot}N{:}N{\cdot}Ph$$

The formation of an azo-compound requires a diazo-radical; and whether this exists for an appreciable time or whether it at once loses nitrogen to give the aryl radical is determined by the degree of positivity of the carbon atom to which the diazonium group is attached. Saunders and Waters (*J.*, 1946, 1154) also assume that, in the action of ammoniacal cuprous oxide on aromatic diazo-compounds, free aryl radicals are intermediates, but that in this case they are formed from undissociated diazo-hydroxide.

In the case of anthranilic acid the mechanism is similar to that for diazotized aniline, the electron from the reducing agent causing the elimination of molecular nitrogen and the formation of a carboxyphenyl radical, two of which unite to form diphenic acid :

$$CO_2H{\cdot}C_6H_4{\cdot}N_2^+ \xrightarrow{e} CO_2H{\cdot}C_6H_4\cdot + N_2$$
$$2CO_2H{\cdot}C_6H_4\cdot \longrightarrow CO_2H{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}CO_2H$$

Since there is no evidence of the formation of the symmetrical azobenzene-2 : 2′-dicarboxylic acid, it is concluded that the carboxybenzenediazonium radical has only a transient existence. This suggests that unsymmetrical azobenzene-2-carboxylic acid resulting from the reduction of a mixture of the diazo-compounds, is formed by the union of a carboxyphenyl radical from the diazotized anthranilic acid and a diazo-cation from the diazotized aniline, the nitrogen of the product being derived from the diazotized aniline :

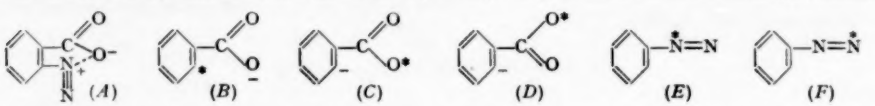
$$CO_2H{\cdot}C_6H_4\cdot + {}^+N_2{\cdot}C_6H_5 \xrightarrow{e} CO_2H{\cdot}C_6H_4{\cdot}N{:}N{\cdot}C_6H_5$$

Atkinson assumed this since, although he suggested no mechanism for the reaction, he stated that " it is apparent that the tendency to form an azo-compound, which diazotized aniline exhibits, predominates over the tendency to form a biaryl which diazotized anthranilic acid exhibits."

In fact the experimental results prove that this cannot be so, and that this mechanism for the reaction is inadequate. The following may be more probable.

It appears that, in the reduction of a mixture of the diazonium compounds, the cation from the diazotized anthranilic acid is capable of combining with a phenyl radical, whereas no azo-compound is produced when diazotized anthranilic acid is reduced by itself. The diazonium salt from anthranilic acid is known to exist as an internal salt (*A*) (Taylor and

Baker, " Sidgwick's Organic Chemistry of Nitrogen," Oxford Univ. Press, 1937, p. 404). Addition of an electron to the group $CO\cdot\bar{O}\ldots\overset{+}{N}_2$ results in disappearance of the electrovalency, elimination of nitrogen, and formation of a carboxyphenyl radical. The latter is mesomeric, having canonical forms such as (*B*—*D*). As in the case of the benzyl radical,



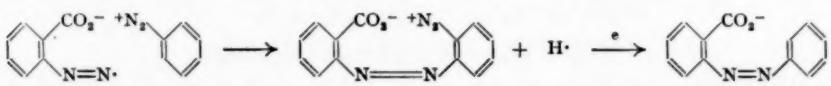
this resonance denotes an appreciable degree of stability and presumably the radical has a long enough life to react with a similar radical to form diphenic acid.

The addition of an electron to a benzenediazonium ion produces a benzenediazonium radical for which also mesomeric forms are possible. Two canonical forms may be written as (*E*—*F*), and others may be derived from the several forms of the benzenediazonium ion enumerated by Dewar (" The Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949, p. 182). When nitrogen is evolved from a benzenediazonium radical a phenyl radical is formed which cannot exhibit mesomerism of the type shown by the carboxyphenyl and the benzenediazonium radical. The phenyl radical is, then, highly reactive but, since diphenyl is not a main reaction product, it does not, apparently, dimerize. It could, either by reaction with water [which is considered improbable (Merz and Waters, *J.*, 1949, 2427)] or by reduction with the cuprammonium salt, form benzene. The benzene is then liable to attack by benzenediazonium radicals with formation of azobenzene. The relevant stages are represented as follows :

$$(1)\quad C_6H_5\cdot N_2^{+} \longrightarrow C_6H_5\cdot N_2\cdot \longrightarrow C_6H_5\cdot + N_2 \longrightarrow C_6H_6$$

$$(2)\quad C_6H_5\cdot N_2\cdot + C_6H_6 \longrightarrow C_6H_5\cdot N{:}N\cdot C_6H_5 + H\cdot$$

Benzenediazonium hydroxide is a stronger base than the amphoteric carboxybenzenediazonium hydroxide and is in excess. In a mixed solution the two would be expected to associate (giving $N\equiv\overset{+}{N}\cdot C_6H_4\cdot C\overset{O}{\underset{O^-}{<}}\ N{:}\overset{+}{N}\cdot C_6H_5$), thus freeing the diazo-group of the carboxybenzenediazonium ions. In this case the reduction of the ion produces a radical which would react intramolecularly with the cation of this ionic complex in a manner similar to that in which a free diazonium radical reacted with benzene in the earlier example :



Loss of nitrogen from the diazonium group of this molecule produces azobenzenecarboxylic acid containing nitrogen atoms previously part of the diazotized anthranilic acid.

On the assumption that a hydrocarbon or equivalent compound, formed by the addition of hydrogen to a free radical, reacts with another free radical, the reaction becomes an extension of the Gomberg reaction (Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2339; Gomberg and Pernert, *ibid.*, 1926, **48**, 1372), for the preparation of unsymmetrical diaryls, which has been proved to proceed with free radicals as intermediates (Waters, " The Chemistry of Free Radicals," Oxford Univ. Press, 1948, p. 153).

In this suggested mechanism a hydrocarbon is initially formed. Traces of hydrocarbon have been isolated in certain reactions (Waters, *J.*, 1937, 2014) and the mechanism advanced by Saunders and Waters (*J.*, 1946, 1154) for the production of these by-products is identical with the initial stages of the mechanism suggested here to explain the main reaction of diazo-salts in alkaline solutions.

We are indebted to Dr. D. H. Tomlin who assayed our nitrogen samples, and to the Department of Scientific and Industrial Research for a grant to one of us (B. I. H.-H.).

THE UNIVERSITY, READING. [*Received, May* 31*st*, 1952.]

816. *The Structure of Native Poly-D-glutamic Acid. Part I.**

By J. Kovács and V. Bruckner.

The poly-D-glutamic acid secreted by *Bacillus subtilis* was converted through the polymethyl ester into the polyhydrazide. After Curtius degradation and subsequent acid hydrolysis of the product, only β-formylpropionic acid (succinic semialdehyde) was found in the hydrolysate, and no αγ-diaminobutyric acid. This suggests that in native poly-D-glutamic acid, γ-glutamyl bonds predominate.

In 1937 Iványovics and Bruckner (*Z. Immunforsch.*, **90**, 304; **91**, 175; *Naturwiss.*, **25**, 250) reported the isolation, from cultures, of the capsular substance responsible for the high virulency of anthrax (Gruber and Futaki, *Münch. Med. Wochenschr.*, 1907, **54**, 249; Preisz, *Zentr. Bakt.*, 1907, **44**, 209); by a technique based on that of Tomcsik and Szongott (*Z. Immunforsch.*, 1932, **76**, 214; 1933, **78**, 86) and of Iványovics and Erdös (*ibid.*, 1937, **90**, 4), they obtained a well-defined substance, the hapten character of which, realised first by Tomcsik and Szongott (*loc. cit.*), made it possible to control further purification by serological reactions. Iványovics (*Zentr. Bakt.*, 1937, **138**, 211) attributed the existing close serological relationship between aërobic sporal microbes and anthrax bacilli to the specific substance of the anthrax capsules, which the microbes of the *subtilis* class convert in the culture medium into a form readily isolable as the insoluble copper salt. The chemical identity of this water-soluble acid substance with the hapten of the anthrax capsules was confirmed by Iványovics and Bruckner (*loc. cit.*) by elementary analysis, neutralisation equivalent, and amino-nitrogen content. The last suggested an approximate molecular weight of 6400—7000 for the *B. subtilis* polypeptide. The identity of the two substances was further demonstrated by acid hydrolysis; in both cases the amino-nitrogen value increased and finally became constant, D-(−)-glutamic acid being the product. The average yield of the hydrochloride was 86% of the value calculated on the assumption that the haptenic polypeptide contains only D-(−)-glutamic acid units, as suggested also by further analytical investigations (Bruckner, Iványovics, and Kovács Oskolás, *Magyar Chem. Foly.*, 1939, **45**, 131; *Chem. Abs.*, 1940, **34**, 3766).

These observations were later confirmed by Bovarnick (*J. Biol. Chem.*, 1942, **145**, 415) and then by Hanby and Rydon (*Biochem. J.*, 1946, **40**, 297), on haptens isolated from *B. subtilis* and from *B. anthracis*, respectively. Hanby and Rydon converted the glutamic acid from acid hydrolysis of *B. anthracis* hapten into pyroglutamic acid, which was quantitatively isolated by chromatography on silica gel. Both the yield and the values obtained from the partition chromatogram of acetylated hydrolysates suggested the presence only of glutamic acid. Although glycine and aspartic acid would remain undetected by this method, the recorded yield of glutamic acid was 99%, proving the absence of other amino-acids. Pongor (*Experientia*, 1950, **6**, 421), using paper chromatography, confirmed this conclusion.

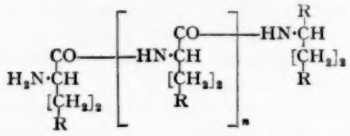
All reports therefore agree that the polypeptide produced by *B. anthracis* and *B. subtilis* is exceptional among the *native* polypeptides in being built up from units of one single amino-acid. Such polypeptides may be termed "monotone polypeptides." (A number of polypeptides of this type have recently been obtained by synthesis; see review by Wieland, *Angew. Chem.*, 1951, **63**, 7.)

Present views on the detailed structure of native poly-D-glutamic acid are conflicting. Iványovics and Bruckner (*loc. cit.*) indicated that the following structural types are to be considered: (*a*) pure α-glutamyl bonds (I*a*), (*b*) pure γ-glutamyl bonds (IV*a*), and (*c*) combinations of both types. Bovarnick (*loc. cit.*) advocated only (IV*a*). Hanby and Rydon (*loc. cit.*) suggested that, in the polyglutamic acid of *B. anthracis*, α-peptide bonds predominate, chains of 50—100 α-bonded D-glutamic acid units being held together by small γ-bonded chains; they noted that the molecular weights of isolated samples were considerably higher (*e.g.*, 53,000) when, in isolation and purification by Iványovics and

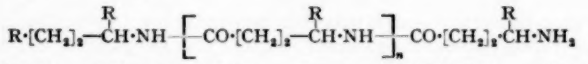
* A preliminary report was published in *Research*, 1952, **5**, 194.

Bruckner's method (*loc. cit.*), the action of acid was kept to a minimum, and they believe that samples of molecular weight **5000—6000**, as investigated by Iványovics and Bruckner, are products of degradation occurring during isolation, and contain only α-glutamyl bonds. It is, however, noteworthy that synthetic α-polyglutamic acid (Hanby, Waley, and Watson, *J.*, 1950, **3239**; Coleman, *J.*, 1950, **3222**) is practically insoluble in water and gives a strongly positive biuret reaction, whereas the native substance is water-soluble and gives no biuret reaction. Also, we find that the optical activity of alkaline solutions of synthetic α-poly-D-glutamic acid decreases quickly owing to racemisation (to be published later), whereas under the same conditions that of the native polypeptide remains unchanged (Bovarnick, *loc. cit.*). Although it may seem relatively less important that synthetic α-poly-D-glutamic acid gives no serological reaction (Hanby, Waley, and Watson, *loc. cit.*)—since in the case of the native substance these reactions may possibly depend on the presence of intermittent γ-peptide-bonded chains—this fact remains nevertheless remarkable in view of the very distinct serological reaction of native poly-D-glutamic acid of low molecular weight (*e.g.*, **6400—7000**), which, according to Hanby and Rydon, would contain only α-glutamyl bondings.

Primarily, our present work was designed to decide, at least qualitatively, whether in native poly-D-glutamic acid the α- or the γ-glutamyl bonds predominate, especially as lack of a reliable method for distinction between the different types of peptide bonds seems to have handicapped structural investigation of proteins (*Ann. Reports*, 1949, **46**, 218).



(I; R = CO_2R') (II; R = CO·NH·NH_2)
(Ia; R = CO_2H) (III; R = NH_2)



(IV; R = CO_2R') (IVa; R = CO_2H) (V; R = CO·NH·NH_2) (VI; R = NH_2)

After conversion of a polyglutamic acid (I*a*) into its methyl ester (I; R′ = Me) and thence into the corresponding polyhydrazide (II), the last would be expected to give on Curtius degradation a monotone polypeptide (III). A glutamic acid of partial structure (IV*a*) would, on the other hand, give ultimately, *via* a polyhydrazide (V), a substance of structure (VI). Now, on hydrolysis a polypeptide (III) would give αγ-diaminobutyric acid, whereas a polypeptide (VI) would give under mild conditions β-formylpropionic acid. If both (I*a*) and (IV*a*) were present in the polypeptide, the hydrolysate would contain both products in a ratio corresponding to that of the α- and γ-glutamyl bonds originally present in the polypeptide.

We have applied this method to native poly-D-glutamic acid prepared by Iványovics and Bruckner's method (*loc. cit.*) from a suitable *B. subtilis* strain. The molecular weight, calculated from van Slyke amino-nitrogen values, was **6400**. On Hanby and Rydon's argument—if this should apply also to the *B. subtilis* polypeptide—α-glutamyl bonds would be expected to predominate. We find, however, that on degradation of **83** mg. of the polyhydrazide no αγ-diaminobutyric acid could be detected in the hydrochloric acid hydrolysate, even as its very insoluble diflavianate, whereas **20** mg. of β-formylpropionic acid could be easily separated from the solution in the form of its *p*-nitrophenylhydrazone. Further, according to Hanby and Rydon's arguments, **83** mg. of a polyhydrazide prepared from polypeptide of molecular weight **6400** should produce no more than **1·0** mg. of β-formylpropionic acid, whereas αγ-diaminobutyric acid should be produced in such quantity that its presence could not have escaped detection, not only as diflavianate but even as the dipicrate.

It is true that in our experiments only **14·5**% of the theoretical quantity of β-formylpropionic acid *p*-nitrophenylhydrazone was isolated which would be expected from polyglutamic acid of structure (IV*a*), but the yield would be decreased by three factors: (*a*) the Curtius degradation of the polyhydrazide is not quantitative; (*b*) β-formylpropionic

acid is rather unstable under the conditions of the acid hydrolysis; and (*c*) the separation of the *p*-nitrophenylhydrazone of this acid is not quantitative. With these limitations, we conclude that in native poly-D-glutamic acid of *B. subtilis* the γ- rather than the α-glutamyl bonding predominates.

We are extending our investigations to native poly-D-glutamic acid of higher molecular weight, prepared from *B. anthracis*, and are refining our method for a reliable assay on the α : γ ratio of the glutamyl bonds by the quantitative determination of ammonia present in the hydrolysate obtained after degradation, 2 equivalents of ammonia being expected to result for each γ-glutamyl bond. Further, experiments to be reported shortly, in which we converted the polymethyl ester into the polyamide, instead of the polyhydrazide, and degraded this amide by Hofmann's method, agree with those now reported.

Experimental

Polymethyl Ester of Native Poly-D-glutamic Acid.—(*a*) *By the action of diazomethane on the polypeptide* (*M*, 6400) *prepared by the original method from* B. subtilis. To the polypeptide, in dilute methanol, ethereal diazomethane was added. From the resulting product a water-insoluble fraction was isolated [Found : OMe, 20·2. Calc., for a polymethyl ester $(C_6H_9O_3N)_n$ corresponding to a polyglutamic acid $(C_5H_7O_3N)_n$ of neutralisation equiv. 129·1 : OMe, 21·7%]. Since our polyacid has a neutralisation equiv. of only 140 (Bruckner, Iványovics, and Kovács Oskolás, *loc. cit.*), an OMe value of 20·1% is theoretically attainable.

(*b*) *By the action of dry methanol and catalytic amounts of acetyl chloride on the polypeptide specified above* (Fraenkel-Conrat, Cooper, and Olcott, *J. Amer. Chem. Soc.*, 1945, **67**, 950; Fraenkel-Conrat and Olcott, *J. Biol. Chem.*, 1945, **161**, 259). The polypeptide (289 mg.) was finely powdered and dried at 100°/1 mm. over phosphoric oxide until of constant weight (45 hours) (Found : Ash, 2·5; amino-N, 0·3%; corresponding to *M*, 4670). To 250 mg. of this substance 4 ml. of dry methanol were added, and the suspension mixed with 0·03 ml. of acetyl chloride and shaken. In 2 hours almost complete dissolution occurred. After 24 hours, the mixture was filtered from a trace of insoluble matter, and to the filtrate 30 ml. of dry ether were added. The viscous gummy precipitate was separated on the centrifuge, redissolved in dry methanol, and reprecipitated with dry ether, then dried in a vacuum-desiccator over phosphoric oxide and paraffin; it was powdered and dried at 100°/1 mm. (P_2O_5). On addition of 15 ml. of water, the product slowly dissolved. The solution was evaporated in the frozen state, and the remaining solid foam was dried at 100°/1 mm. (P_2O_5), giving an almost colourless amorphous powder (247 mg.) (Found : OMe, 19·7%).

(*c*) *By the action of methanolic hydrogen chloride on the sodium salt of the polypeptide.* From cultures of *B. subtilis* the copper salt of the polypetide was isolated by the usual method, and dialysed against citrate buffer solution (0·5M, pH 5·0), and then against distilled water (see Bovarnick, *loc. cit.*). The solution was finally evaporated *in vacuo* and the dry powdered product was dried to constant weight (200 hours) at 100°/1 mm. (P_2O_5) (Found : Ash, 18%). To 500 mg. of this substance 15 ml. of absolute methanol and then 0·4 ml. of concentrated hydrochloric acid were added, and the mixture shaken for 5 hours, complete dissolution occurring. By next morning a gel was formed. This was mixed with 45 ml. of absolute methanol and then centrifuged. After decantation, the residue was mixed with 30 ml. of absolute methanol and again centrifuged. The combined methanolic solutions were concentrated *in vacuo* to 3 ml., and mixed with absolute ether until no more precipitate formed. The precipitate was then separated on the centrifuge, redissolved in methanol, and reprecipitated with ether. After being separated on the centrifuge, the substance was washed with ether, dried in a vacuum-desiccator, powdered, and dried to constant weight (16 hours) at 100°/1 mm. over phosphoric oxide. It formed an almost colourless, water-soluble, amorphous powder (Found : Ash, 4; OMe, 20·1; total N, 9·3; amino-N, 0·31%, corresponding to *M*, 4500).

Polyhydrazide of Native Poly-D-glutamic Acid.—(i) A solution of the polymethyl ester (96 mg.) in anhydrous hydrazine (3 ml.) was kept for 3 days and then completely evaporated at 0·001 mm., liquid air being used for cooling. The powdered residue was dried in a vacuum-desiccator for 8 days and then at 78°/1 mm. over phosphoric oxide for 6 hours. It formed a nearly colourless powder (95 mg.) insoluble in water and completely soluble in dilute hydrochloric acid (Found : OMe, 0·0; total N, 26·6. Calc. from OMe content of starting material : total N, 29·9%).

(ii) The polymethyl ester (240 mg.) was converted into polyhydrazide, as described in (i) except that, after evaporation of the hydrazine solution, the residue was ground with 6 ml. of water, and dried in the frozen state and then at 100°/1 mm. over phosphoric oxide (48 hours).

The properties of the substance (240 mg.) were similar to those described under (i) (Found: total N, 26·7%). In a repetition of this procedure 280 mg. of polyester afforded 278 mg. of polyhydrazide (Found: total N, 28·1%).

Degradation of the Polyhydrazide of Native Poly-D-glutamic Acid.—(i) To a solution of 83 mg. of the polyhydrazide, obtained as in (i), above, water (1 ml.) and N-hydrochloric acid (1·2 ml.), sodium nitrite solution (1·974%; 1·86 ml.) was slowly added (10 minutes) with ice-cooling and shaking. Fine gummy particles of the polyhydrazide separated. When the mixture was warmed over a micro-burner with N-sodium hydroxide solution (0·7 ml.) for 1—2 minutes, foaming occurred and the substance was deposited on the walls of the flask. The liquid (*A*) was removed by decantation, the remaining solid dissolved in concentrated hydrochloric acid (4·5 ml.), and the solution heated under gentle reflux for 2 hours.

1 Ml. of this solution was evaporated *in vacuo*, and the residue (12 mg.) dissolved in two drops of water and mixed with 3 drops of saturated aqueous picric acid; no crystallisation occurred after long storage, or even after seeding with crystals of αγ-diaminobutyric acid dipicrate.

Another 1 ml. of the above hydrolysate was evaporated, and the residue mixed with 2 drops of a freshly prepared and filtered solution of *p*-nitrophenylhydrazine in N-hydrochloric acid. Instant precipitation of golden-yellow flocks occurred. These were filtered off, washed with 1 ml. of cold water, and dried first in a vacuum-desiccator, then at 100°/1 mm. over phosphoric oxide; 3·4 mg. of yellow needles were obtained; they melted at 178° alone or mixed with an authentic specimen of β-formylpropionic acid *p*-nitrophenylhydrazone, in agreement with the literature (Harries, *Ber.*, 1912, **45**, 2585).

The turbid solution (*A*), above, was mixed with an equal volume of concentrated hydrochloric acid, refluxed for 2 hours, set aside for 4 days, and finally evaporated *in vacuo* to dryness. The residue was redissolved in 1 ml. of a freshly prepared solution of *p*-nitrophenylhydrazine in N-hydrochloric acid; needles of the *p*-nitrophenylhydrazone instantly separated. These were filtered off, washed repeatedly with cold water, and dried (P_2O_5), the product (5 mg.) melting at 174° undepressed by authentic β-formylpropionic acid *p*-nitrophenylhydrazone. The total yield of the latter is therefore $4·5 \times 3·4 + 5·0 \simeq 20$ mg. from 83 mg. of the polyhydrazide, corresponding to a 14·5% yield from 137·8 mg. of pure γ-polypeptide starting material.

(ii) A solution of the polyhydrazide (50 mg.) in 0·1N-hydrochloric acid (3·2 ml.) was treated with 1·76% sodium nitrite solution as described under (i). The mixture containing natant polyazide precipitate was mixed with concentrated hydrochloric acid (5 ml.) and warmed until the solution became clear. This was evaporated *in vacuo* to dryness, and the residue redissolved in concentrated hydrochloric acid (5 ml.), then refluxed for 90 minutes, and again freed from water *in vacuo*. This procedure was repeated, and the residue then mixed with 7 ml. of a freshly prepared solution of *p*-nitrophenylhydrazine in N-hydrochloric acid. The yellow crystals were filtered off, washed with 1·5 ml. of cold water, and dried at 100°; the yield was 11 mg., or 13·2% of the quantity calculated as above and the m. p. 175°. After one recrystallisation (giving 6·6 mg.) from 4 ml. of water the m. p. rose to 180°, undepressed by admixture of an authentic specimen (Found: C, 50·9; H, 4·6. Calc. for $C_{10}H_{11}O_4N_3$: C, 50·6; H, 4·7%).

(iii) A solution of polyhydrazide (195 mg.) in 0·2N-hydrochloric acid (5 ml.) was converted into a suspension of the polyazide as described above under (i), N-sodium hydroxide solution (1·6 ml.) was added, and the mixture warmed for 15 minutes on the steam-bath; it was then acidified with concentrated hydrochloric acid (11 ml.) and refluxed for 2 hours. The pale yellow solution was evaporated *in vacuo*, the residue redissolved in water (5 ml.), and the solution again evaporated. This procedure was repeated, then the residue was dissolved in 20 ml. of water, and the solution halved.

One half was concentrated to 2 ml., and a solution of phosphotungstic acid (2 g.) in water (3 ml.) was added. Instantly, copious precipitation occurred, and the precipitate was separated, and treated in an open flask with gently boiling barium hydroxide solution. The mixture was filtered, barium ions precipitated with dilute sulphuric acid, and the filtrate concentrated *in vacuo* to a small volume, and mixed with 2 ml. of a concentrated solution of flavianic acid. No precipitation occurred on long storage, and the solution remained clear after being seeded with crystals of αγ-diaminobutyric acid diflavianate.

The other half of the above solution was evaporated, and the *p*-nitrophenylhydrazone of β-formylpropionic acid was precipitated as usual.

Control Experiments on the Precipitation of β-Formylpropionic Acid as its p-Nitrophenylhydrazone.—Small amounts of crystalline β-formylpropionic acid, m. p. 147°, were investigated as to their precipitability as *p*-nitrophenylhydrazone, and the influence of the acid hydrolysis upon this procedure. (i) β-Formylpropionic acid (7 mg.) was dissolved in 1 drop of N-hydro-

chloric acid and 4 drops of the reagent; on gentle warming, the solution solidified to a mass of crystals, which were filtered off and washed with 5 ml. of cold water; the dry product weighed 11·2 mg. (68·9%).

(ii) A solution of β-formylpropionic acid (9 mg.) and sodium chloride (11 mg.) in water (3 ml.) mixed with concentrated hydrochloric acid (3 ml.) was evaporated *in vacuo*, and the residue was redissolved in 7 drops of the reagent. The product, after collection, washing, and drying, weighed 10 mg. (47·8%).

(iii) A solution of β-formylpropionic acid (7 mg.) and sodium chloride (7 mg.) in concentrated hydrochloric acid (2 ml.) was refluxed for 2 hours, set aside for 2 hours, and then evaporated *in vacuo* to dryness. The residue was redissolved in a small amount of water, which was distilled off *in vacuo*. On dissolution of the residue in 4 ml. of the reagent, crystallisation occurred after seeding. The product, isolated as usual, weighed 2 mg. (12·3%).

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817. *The Reactions of Metallic Salts of Acids with Halogens. Part III.* Some Reactions of Salts of Fluorohalogenoacetates† and of Perfluoro-acids.*

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Reaction of silver salts of fluorohalogeno-acids † with chlorine, bromine, or iodine constitutes a general method for the synthesis of fluorohalogenohydrocarbons, and is exemplified by the preparation of the new compounds CHClIF, CHBrIF, $CClBr_2F$, CCl_2BrF, CCl_2IF, $CClBrF_2$, and $CClIF_2$. The stability of the silver salts of incompletely halogenated fluoro-acids and of fluorohalogenomethanes is considered. The silver salt reaction applied to the perfluoroalkanecarboxylic acids yields a series of perfluoroalkyl chlorides, bromides, and iodides, $CF_3{\cdot}[CF_2]_n{\cdot}X$ (X = Cl, Br, or I; n = 1—6). The sodium salts of the perfluoro-acids decompose when heated, giving high yields of the perfluoroalk-1-enes, and a mechanism for this general reaction is advanced. Conversion of chlorotrifluoroethylene into bromotrifluoroethylene is described.

SILVER TRIFLUOROACETATE with an excess of chlorine, bromine, or iodine gives high yields of the trifluoromethyl halide (Part I, *J.*, 1951, 584):

$$CF_3{\cdot}CO_2Ag + X_2 \longrightarrow CF_3X + CO_2 + AgX$$

The present communication (cf. *Nature*, 1950, **166**, 192; 1951, **168**, 1028; Abs. 75th Anniversary Meeting, Amer. Chem. Soc., New York, September, 1951) shows that the method is general, since the silver salts of the fluorohalogenoacetic acids, $CHXF{\cdot}CO_2H$ (X = H, Cl, Br, or I), $CF_2Y{\cdot}CO_2H$ (Y = H, Cl, or Br), $CCl_2F{\cdot}CO_2H$, and $CClBrF{\cdot}CO_2H$, produce the compounds shown in Table 1 when treated with the appropriate halogen (new compounds marked *).

TABLE 1.

CH_2ClF	CH_2BrF	CH_2IF	$CHCl_2F$	$CHClBrF$	$CHClIF$*	$CHBr_2F$	$CHBrIF$*	CHI_2F
$CHClF_2$	$CHBrF_2$	$CHIF_2$						
$CClBr_2F$*	CCl_2BrF*	CCl_2F	CCl_2IF*	CBr_2F_2	CCl_2F_2	$CClBrF_2$	$CClIF_2$*	

The temperature required for iodination is low when Y and Z in $CYZF{\cdot}CO_2Ag$ are strongly electronegative (*e.g.*, F), but increases when Y and Z = H, etc., until decarboxylation with simultaneous iodination is accompanied by thermal decomposition of the silver salt. The nature of Y and Z also affects the yield of the iodohalogenomethane. Thus, when Y = F, the yields fall off markedly for change of Z, in the order F > Cl > Br. This is attributed to the weakening of the carbon–iodine bond in $CZIF_2$ by steric effects as well as by the decrease in negativity of Z. The steric effect becomes more apparent as Y increases in size, and yields of CZBrIF are low even when Z = H.

* Part II, *J.*, 1952, 993.

† In the sense used here, " halogen " excludes fluorine.

If the silver salt reaction involves a free-radical mechanism:

$$CYZF{\cdot}CO_2Ag \xrightarrow{X_2} CYZF{\cdot}CO_2X \longrightarrow CYZF{\cdot} + CO_2 + X{\cdot} \qquad CYZF{\cdot} \xrightarrow{X_2} CXYZF$$

then the ease of formation and reactivity of the CYZF· radical will be important in determining yields. Evidence to be presented in another paper shows that the order of radical reactivities is CBr_2F, CCl_2F, $CClF_2$, $CHClF < CHF_2$, CF_3, C_2F_5, etc. In this connection it may be noted that the CHClF, CCl_2F, and $CClF_2$ radicals derived from the corresponding iodides (Table 1) are substantially inert to glass and give high yields of the dimers $C_2H_2Cl_2F_2$, $C_2Cl_4F_2$, and $C_2Cl_2F_4$, whereas the CHF_2 radical undergoes some dimerisation but also gives silicon tetrafluoride and carbon dioxide. Under comparable conditions the CF_3 radical attacks glass readily to given silicon tetrafluoride and carbon monoxide and dioxide, and only small amounts of hexafluoroethane (*J.*, 1949, 2948; 1950, 3041).

Improved routes to some of the acids have been developed. Thus, Swarts's method for bromofluoroacetic acid (*Bull. Acad. roy. Belg.*, 1899, **37**, 357; *Zentr.* 1899, II, 281; see Experimental) has been replaced by the synthesis:

$$CF_2{:}CClF \xrightarrow{HCl} CClF_2{\cdot}CHClF \xrightarrow{Zn\text{–}EtOH} CF_2{:}CHF \xrightarrow{Br_2} CBrF_2{\cdot}CHBrF$$

$$CBrF_2{\cdot}CHBrF \xrightarrow[EtOH]{KOH\text{–}} CF_2{:}CBrF \xrightarrow{EtO^-} EtO{\cdot}CF_2{\cdot}CHBrF \xrightarrow{H^+}$$

$$CHBrF{\cdot}CO_2Et \longrightarrow CHBrF{\cdot}CO_2H$$

Chlorotrifluoroethylene is readily converted into bromotrifluoroethylene by the route shown. The ready base-catalysed addition of ethanol to the bromo-olefin again reveals the susceptibility of a polyfluoro-olefin to nucleophilic attack. The direction of addition accords with that of hydrogen chloride to give 1-bromo-2-chloro-1 : 2 : 2-trifluoroethane. The fluorobromo-ether is isomeric with that ($CBrF_2{\cdot}CHF{\cdot}OEt$) obtained by Swarts (see "Organic Reactions," John Wiley, New York, 1944, Vol. II, p. 87) from 1 : 2-dibromo-1 : 2 : 2-trifluoroethane, and thus shows that Swarts's ether arose by direct replacement of bromine by ethoxide rather than by the alternative dehydrohalogenation route:

$$CBrF_2{\cdot}CHBrF \xrightarrow{NaOEt} CF_2{:}CBrF \xrightarrow{EtO^-} EtO{\cdot}CF_2{\cdot}CHBrF$$

The marked lability of fluorine atoms adjacent to an ether link was noted and applied by Swarts, and is further exemplified by the acid hydrolysis of the bromofluoro-ether to ethyl bromofluoroacetate.

Bromofluoroacetic acid was also used to synthesise bromochlorofluoroacetic acid:

$$CHBrF{\cdot}CO_2H \longrightarrow CHBrF{\cdot}COCl \xrightarrow[light]{Cl_2} CClBrF{\cdot}COCl \longrightarrow CClBrF{\cdot}CO_2H$$

Dichlorofluoroacetic acid was similarly prepared from chlorofluoroacetic acid (see Experimental).

The silver salts of chloro- and bromo-fluoroacetic acid and of chlorodifluoroacetic acid are unstable to water. The first two are quantitatively converted into glyoxylic acid and its silver salt, halide, and fluoride; the third yields oxalic acid, chloride, and fluoride. The most probable reaction is formation of a CHF·OH or $CF_2{\cdot}OH$ group which in an aqueous medium is unstable (*Nature*, 1951, **168**, 1028) and loses hydrogen fluoride:

$$CHBrF{\cdot}CO_2Ag \xrightarrow{H_2O} Br^- + HO{\cdot}CHF{\cdot}CO_2Ag \xrightarrow{-HF} CHO{\cdot}CO_2Ag \xrightarrow[-HF]{Br^-} CHO{\cdot}CO_2H + AgBr$$

$$CClF_2{\cdot}CO_2Ag \xrightarrow{H_2O} Cl^- + HO{\cdot}CF_2{\cdot}CO_2Ag \xrightarrow{-HF} F{\cdot}CO{\cdot}CO_2Ag \xrightarrow[-HF]{Cl^-} (CO_2H)_2 + AgCl$$

Fluorohalogenomethanes which contain one hydrogen atom (*e.g.*, CHClIF, CHI_2F) are decomposed completely by alcoholic potassium hydroxide to halide and formate; some of those which are hydrogen-free (*e.g.*, CCl_2IF, $CClBr_2F$) are completely decomposed to halide and carbonate. Other polyhalogenomethanes ($CClIF_2$ and $CHIF_2$) give the compounds in which iodine has been replaced by hydrogen, as well as being decomposed to halide and carbonate, whereas the perfluoroalkyl iodides (*e.g.*, C_3F_7I) give the corresponding hydrogeno-

compound in high yield. These observations suggest that in the fluorohalogenomethane series two mechanisms can operate: (*a*) nucleophilic attack on carbon, *e.g.*,

$$OH^- \overset{+}{\curvearrowright} CHClF\text{—}\overset{\curvearrowright}{I} \longrightarrow HO{\cdot}CHClF\ (+I^-) \xrightarrow{-HF} H{\cdot}COCl \xrightarrow{KOH} H{\cdot}CO_2K$$

which predominates when the compound contains hydrogen, *i.e.*, resembles an alkyl halide; and (*b*) nucleophilic attack on iodine or bromine, *e.g.*,

$$OH^- \overset{+}{\curvearrowright} I\text{—}\overset{\curvearrowright}{C}ClF_2 \longrightarrow HOI + CClF_2^- \xrightarrow{Solvent} CHClF_2$$

It appears that (*b*) only becomes important when two or more fluorine atoms are present, since chlorodifluoroiodomethane and difluoroiodomethane (where chlorodifluoromethane and difluoromethane are stable to bases) give carbonate and halide and only low yields of the hydrogeno-compounds. Thus either the intermediate ions ($CClF_2^-$, CHF_2^-) are unstable, or carbonate is formed *via* (*a*):

$$OH^- \overset{+}{\curvearrowright} CClF_2\text{—}\overset{\curvearrowright}{I} \longrightarrow HO{\cdot}CClF_2\ (+\ I^-) \xleftarrow{-HF} F{\cdot}COCl \xrightarrow{KOH} F^- + CO_3^=$$

Increase in the positive character of the iodine or bromine atoms will facilitate (*b*), and the yield of the hydrogeno-compound is at a maximum with the perfluoroalkyl iodides.

The formation of the ether $CF_3{\cdot}CHF{\cdot}CF_2{\cdot}OEt$ during hydrolysis of heptafluoroiodopropane is in accord with the intermediate formation of the $C_3F_7^-$ ion:

$$OH^- \overset{+}{\curvearrowright} I\text{—}\overset{\curvearrowright}{C}F_2{\cdot}CF_2{\cdot}CF_3 \longrightarrow HOI + C_3F_7^-$$

$$\overset{\curvearrowleft}{F}\text{—}CF(CF_3)\text{—}\overset{\curvearrowleft}{C}F_2^- \longrightarrow F^- + C_3F_6 \xrightarrow{EtO^-} CF_3{\cdot}CHF{\cdot}CF_2{\cdot}OEt$$

For other evidence for the decomposition of fluorocarbanions into olefins see *Nature*, 1951, **168**, 1028, *J.*, 1952, 3423, and below.

The silver salt reaction, applied to the higher perfluoro-acids, $CF_3{\cdot}[CF_2]_n{\cdot}CO_2H$, where $n = 1$—6, gives the corresponding halides, $CF_3{\cdot}[CF_2]_n{\cdot}X$, in excellent yield. The compounds where X = Cl or Br are inert, like chloro- or bromo-trifluoromethane; those where X = I undergo free-radical reactions of the type described earlier for trifluoroiodomethane, but have the advantage that they can be manipulated in conventional apparatus.

Silver trifluoroacetate reacts with halogens *via* the intermediate $CF_3{\cdot}CO_2X$ (Part II, *loc. cit.*). The reactions of phosphorus, sulphur, or mercury with silver trifluoroacetate were investigated with the object of preparing perfluoroalkyl derivatives (*J.*, 1949, 2953; 1952, 2198, 2549, 3552) without the intermediate formation of the fluoro-iodide:

$$m CF_3{\cdot}CO_2Ag + 2M \longrightarrow (CF_3{\cdot}CO_2)_mM + Ag_mM$$
$$(CF_3{\cdot}CO_2)_mM \longrightarrow (CF_3)_mM + mCO_2$$

The perfluoroalkyl derivatives were not obtained. Phosphorus gave silver phosphide but only a trace of carbon dioxide, and the product was trifluoroacetic anhydride, which was also formed, with sulphur dioxide, when the silver salt was heated with sulphur:

$$4CF_3{\cdot}CO_2Ag + 3S \longrightarrow 2Ag_2S + 2(CF_3{\cdot}CO)_2O + SO_2$$

Attempts to prepare trifluoromethyl arsenicals and phosphines by the interaction of silver trifluoroacetate and arsenic or phosphorus iodides, *i.e.*, to produce trifluoroiodomethane *in situ*, were unsuccessful.

An alternative but less convenient route to trifluoroiodomethane from trifluoroacetic acid is to convert the latter into the anhydride which, with an excess of iodine, yields the fluoro-iodide, carbon dioxide, and carbon monoxide, probably by C–O fission:

$$(CF_3{\cdot}CO)_2O + I_2 \longrightarrow CF_3{\cdot}CO_2I + CF_3{\cdot}COI$$

followed by the known decarboxylation and decarbonylation reactions of iodine trifluoroacetate and trifluoroacetyl iodide (Part I). Bromine or chlorine failed to convert trifluoroacetyl chloride into bromo- or chloro-trifluoromethane.

Sodium or potassium trifluoroacetate yield CXF_3 when heated with halogen, X_2, at

temperatures higher than those required for silver trifluoroacetate (Part I). Attempts to repeat this with sodium heptafluorobutyrate gave only moderate yields of C_3F_7X, and the main product was 1 : 2-dibromohexafluoropropane (X = Br) or hexafluoropropene (X = I); sodium pentafluoropropionate similarly yielded 1 : 2-dibromotetrafluoroethane, or 1 : 2-diiodotetrafluoroethane and perfluoro*cyclo*butane (by thermal dimerisation of tetrafluoroethylene), and only small amounts of bromopentafluoroethane or pentafluoroiodoethane. Two reactions are involved : (*a*) reaction of halogen with the sodium salt by a mechanism, probably of free-radical type [see (*b*)], analogous to that for the silver salt, leading to the formation of C_2XF_5 or C_3XF_7; and (*b*) decarboxylation (independently of halogen) of the sodium salt of the perfluoro-acid to an olefin which reacts further with bromine or, in the case of tetrafluoroethylene, with iodine. Reaction (*b*) is of general application for the preparation of alk-1-enes from the perfluoro-acid, and was independently discovered and developed by the Minnesota Mining and Manufacturing Co. (personal communication). It may be interpreted by the instability of the fluorocarbanion :

$$CF_3\cdot[CF_2]_n\cdot CF_2\cdot CF_2\cdot CO_2Na \longrightarrow CF_3\cdot[CF_2]_n\cdot CF_2\cdot CF_2^- + CO_2 + Na^+$$

$$F\text{—}CF(\text{—}[CF_2]_n\cdot CF_3)\text{—}CF_2^- \longrightarrow CF_3\cdot[CF_2]_n\cdot CF{:}CF_2 + F^-$$

and with suitable technique gives yields of 60—90%. The data shown in Table 2 for the

TABLE 2.

$CF_3\cdot[CF_2]_n\cdot CF_2\cdot CF_3$	C_3F_8	C_4F_{10}	C_5F_{12}	C_7F_{16}	C_8F_{18}
B. p.	−38°	−5°	51°	82°	103°
$CF_3\cdot[CF_2]_n\cdot CF{:}CF_2$	C_3F_6	C_4F_8	C_5F_{12}	C_7F_{14}	C_8F_{16}
B. p.	−29°	i°	57°	83°	105°
Fluoro*cyclo*alkane	—	C_4F_8	C_5F_{12}	—	—
B. p.	—	−4°	52°	—	—
Fluoro*cyclo*alkene	—	C_4F_6	C_5F_{10}	—	—
B. p.	—	i°	54°	—	—

fluoro-olefins so prepared show that cyclisation or introduction of a double bond into a fluoro-carbon produces little change in boiling point.

The influence of the perfluoroalkyl group on the adjacent $CF{:}CF_2$ group is being studied. Its presence is shown by its characteristic C=C stretching vibration in the infra-red at 5·56 μ (*J.*, 1952, paper No. 849), and by oxidation to give the fluoro-acid containing two carbon atoms fewer than originally, *e.g.*,

$$CF_3\cdot[CF_2]_6\cdot CO_2Na \longrightarrow CF_3\cdot[CF_2]_4\cdot CF{:}CF_2 \xrightarrow{KMnO_4} CF_3\cdot[CF_2]_4\cdot CO_2H$$

Descent of the homologous fluoro-acid series is thus possible as well as ascent *via* the fluoro-iodides (*Nature*, 1950, 192).

EXPERIMENTAL

The silver salt reaction was carried out with the acids shown below. Molecular weights were determined by Regnault's vapour-density method.

Monofluoroacetic Acid.—To a stirred suspension of silver carbonate in water (100 ml.) was added a 3% excess of monofluoroacetic acid (10·0 g.). The mixture was heated to 70°, then cooled, and the insoluble *silver monofluoroacetate* (86%) (Found : Ag, 58·1. $C_2H_2O_2FAg$ requires Ag, 58·3%) was dried *in vacuo* over phosphoric oxide. The silver salt is more easily prepared by the addition of excess of N-silver nitrate to aqueous sodium fluoroacetate. The silver salt (9·2 g.) was heated in a sealed tube with chlorine (10% excess) from 50° to 120° during 5 hours, to give, after fractionation of the products *in vacuo*, chlorofluoromethane (52%), b. p. 8·5° (Found : C, 17·7%; *M*, 68. Calc. for CH_2ClF : C, 17·5%; *M*, 68·5). Henne (*J. Amer. Chem. Soc.*, 1937, **59**, 1400) reports b. p. −9·0°. Treatment with bromine (5% excess) similarly yielded bromofluoromethane (62%), b. p. 17·5° (Found : C, 10·6%; *M*, 113. Calc. for CH_2BrF : C, 10·6%; *M*, 113). Swarts, *Bull. Acad. roy. Belg.*, 1910, **58**, 113, reports b. p. 18—20°. Silver monofluoroacetate (8·1 g.) and iodine (150% excess), premixed in a silica flask, were slowly heated to 180—260°. The products were continuously removed by pumping through a trap cooled in liquid air to prevent decomposition of the fluoroiodomethane (55%),

b. p. 52—53°, n_D^{20} 1·490 (Found: C, 7·8; H, 1·4%; *M*, 159. Calc. for CH_2IF: C, 7·5; H, 1·3%; *M*, 160). Van Arkel and Zanetsky (*Rec. Trav. chim.*, 1937, **56**, 167) report b. p. 53·4°. The compound readily liberates iodine on exposure to light.

Chlorofluoroacetic Acid.—This was prepared in improved yield by slight modification of Young and Tarrant's procedure (*J. Amer. Chem. Soc.*, 1949, **71**, 2432). Treatment of chlorotrifluoroethylene (20 g.) with excess of ethanol and sodium ethoxide (2%) yielded 2-chloro-1 : 1 : 2-trifluoroethyl ethyl ether (96%), b. p. 88°, which was hydrolysed in a steel vessel by treatment with a three-fold excess of concentrated sulphuric acid at 0—5° during 4 hours. The temperature was raised to 50°, and the volatile material, removed by pumping through a cold trap, was washed with ice-water and distilled from phosphoric oxide, to give ethyl chlorofluoroacetate (81%), b. p. 128°, hydrolysed by 10% aqueous sodium hydroxide to chlorofluoroacetic acid (64%), b. p. 160·5—161°. The acid (10·3 g., 5% excess) was treated with anhydrous silver oxide and a little phosphoric oxide in a sealed tube with vigorous shaking, the temperature being raised slowly to 50°, to give *silver chlorofluoroacetate* (87%) (Found: Cl, 16·1; Ag, 48·7. C_2HO_2ClFAg requires Cl, 16·2; Ag, 49·2%).

When silver chlorofluoroacetate (0·010 mole) was stirred with water in a Polythene beaker for 3 weeks, silver chloride (0·006 mole), unchanged silver chlorofluoroacetate (0·001 mole), silver glyoxylate (0·002 mole) and glyoxylic acid (0·006 mole) were identified as follows. The reaction mixture gave a filtrate *A* and solid products *B*. *B* was dried *in vacuo* over phosphoric anhydride, and the silver chlorofluoroacetate in it was estimated by fusion of a portion with an excess of sodium followed by determination of fluoride. To a second portion of *B* was added dilute nitric acid, and the solution was concentrated *in vacuo* to remove chlorofluoroacetic acid; the concentrate was warmed with concentrated nitric acid and after dilution with water the residual silver chloride was weighed. In this experiment, silver glyoxylate in *B* was estimated by difference. In a second experiment, *B* was treated with a further quantity of water to complete the destruction of the silver chlorofluoroacetate, and the solid then removed by filtration was shown to consist of only silver glyoxylate and silver chloride by decomposition of the former with hydrochloric acid, filtration, and evaporation of the filtrate *in vacuo* over phosphoric anhydride; qualitative tests, and estimation as the calcium salt (see below), showed only glyoxylic acid. The filtrate *A* was freeze-dried in a Polythene beaker, and qualitative examination of the aqueous solution revealed only fluoride ion and no organic material. The residue from *A* was a viscous liquid which did not crystallise on further drying *in vacuo* over phosphoric anhydride and analysed as $CHO{\cdot}CO_2H$ (Found: C, 31·9; H, 2·7. Calc. for $C_2H_2O_3$: C, 32·4; H, 2·7%). A portion of the oil heated at 100° with sodium hydroxide was shown qualitatively to give glycollic and oxalic acids. A second portion yielded an oxime, m. p. 142° (decomp.) (lit., 143°). The remainder of the oil was dissolved in water and precipitated by addition of calcium chloride solution as calcium glyoxylate (97%), weighed as $(CHO{\cdot}CO_2)_2Ca,2H_2O$ (Doebner and Glass, *Annalen*, 1901, **317**, 417) (Found: Ca, 17·9. Calc. for $C_4H_8O_9Ca$: Ca, 18·0%). Control experiments with pure glyoxylic acid and with an artificial mixture showed that the above methods of analysis were reliable to ±3%. In a third experiment, one half of the filtrate *A* was used for estimation of fluoride as fluorosilicic acid (Found: F^-, equiv. to 97% of the silver salt decomposed), and the second portion was used for estimation of glyoxylic acid as its calcium salt (98% theor.).

The silver salt (3·1 g.), treated with chlorine or bromine as described for silver fluoroacetate, gave dichlorofluoromethane (73%) (Found: *M*, 103. Calc. for $CHCl_2F$: *M*, 103), b. p. 9° (Swarts, *Bull. Acad. roy. Belg.*, 1892, **24**. 474, reports b. p. 8·9°), and bromochlorofluoromethane (67%) (Found: *M*, 146. Calc. for CHBrClF: *M*, 147·5), b. p. 36·5° (*idem*, *ibid.*, 1893, **26**, 102, reports b. p. 38°), respectively. The silver salt (4·2 g.) with iodine (see silver fluoroacetate) gave *chlorofluoroiodomethane* (35%) (Found: C, 5·7; H, 0·5; F, 9·8%; *M*, 193. CHClFI requires C, 6·2; H, 0·5%; F, 9·8%; *M*, 194·5) as a light-sensitive liquid, b. p. 35°/150 mm. (*ca.* 76°/760 mm.). When shaken vigorously with mercury and exposed to ultra-violet radiation, chlorofluoroiodomethane (0·9 g.) was converted into 1 : 2-dichloro-1 : 2-difluoroethane (79%), b. p. 59°, n_D^{25} 1·390 (Found: *M*, 135. Calc. for $C_2H_2Cl_2F_2$: *M*, 135). Henne and Waalkes (*J. Amer. Chem. Soc.*, 1945, **67**, 1639) report b. p. 59°. Thermal decomposition at 230° also gave 1 : 2-dichloro-1 : 2-difluoroethane (57%).

Bromofluoroacetic Acid.—Bromotrifluoroethylene was prepared in 78% yield by debromination of 1 : 1 : 2-tribromotrifluoroethane with zinc and ethanol (Swarts, *loc. cit.*) or preferably as follows. Chlorotrifluoroethylene was converted into 1 : 2-dichlorotrifluoroethane (96%) by anhydrous hydrogen chloride and a catalytic amount of aluminium chloride at 150° in an autoclave. The product (Found: *M*, 153. Calc. for $C_2HCl_2F_3$: *M*, 153), b. p. 28°, n_D^{20} 1·335

(Henne and Ladd, *J. Amer. Chem. Soc.*, 1936, **58**, 402, report b. p. 28°), was dechlorinated by zinc and refluxing ethanol in an apparatus fitted with reflux condenser held at −45°, to give trifluoroethylene (86%), b. p. −55° (Found: *M*, 82. Calc. for C_2HF_3: *M*, 82). Swarts (*Bull. Acad. roy. Belg.*, 1899, **37**, 357) reports b. p. −51°. The olefin absorbed bromine under the influence of ultra-violet light to give quantitatively 1 : 2-dibromotrifluoroethane, b. p. 75·8° (Swarts, *loc. cit.*, reports b. p. 76°), n_D^{25} 1·418 (Found: *M*, 240. Calc. for $C_2HBr_2F_3$: *M*, 242), 18·6 g. of which were stirred and cooled in ethanol (30 ml.) to 0° in a flask fitted with reflux water-condenser. After the slow addition of *ca.* 90% of the theoretical amount of ice-cold 10% ethanolic potassium hydroxide, the whole was heated to 30° for 10 minutes, then cooled to 0°, and a further amount of base added (10% excess finally) and the temperature was raised to the b. p. The volatile products were washed with water and fractionated *in vacuo*, to give bromotrifluoroethylene (77%), b. p. −4·5° (Found: C, 14·9%; *M*, 160. Calc. for C_2BrF_3: C, 14·9%; *M*, 161). Swarts (*loc. cit.*) reports b. p. −2·5°.

Bromotrifluoroethylene (2·1 g.), heated with anhydrous hydrogen chloride (10% excess) at 150—180° for 12 hours, gave 1-*bromo*-2-*chloro*-1 : 2 : 2-*trifluoroethane* (63%), b. p. 51—52° (Found: C, 12·4; H, 0·3%; *M*, 196. $C_2HBrClF_3$ requires C, 12·2; H, 0·5%; *M*, 197·5), dehalogenated in 85% yield to trifluoroethylene.

Bromotrifluoroethylene (10·9 g.) was slowly bubbled into a stirred solution of ethanol (150 ml.) containing 0·2% of sodium ethoxide at −10°, to give, after addition of water, etc., 2-*bromo*-1 : 1 : 2-*trifluoroethyl ethyl ether* (83%), b. p. 108°, n_D^{20} 1·375 (Found: C, 23·4; H, 2·9%; *M*, 200—210. $C_4H_6OBrF_3$ requires C, 23·2; H, 2·9%; *M*, 207). Temperature control is important, since if the sodium ethoxide is destroyed by reaction with the bromofluoro-ether, the addition reaction stops. By treatment with a three-fold excess of concentrated sulphuric acid at −5° in a steel vessel containing ground glass, the ether yielded ethyl bromofluoroacetate (56%), converted into bromofluoroacetic acid (61%), b. p. 106°/35 mm. (Found: equiv., 156·5. Calc. for $C_2H_2O_2BrF$: equiv., 157); Swarts, *loc. cit.*, reports b. p. 183°. *Silver bromofluoroacetate* (84%) (Found: Br, 30·1; Ag, 40·5. C_2HO_2BrFAg requires Br, 30·3; Ag, 40·9%) was prepared as was silver chlorofluoroacetate. The silver salt (0·01 mole) was decomposed by water during 14 days to give silver bromide (0·009 mole), silver glyoxylate (0·001 mole), and glyoxylic acid (0·008 mole), and, in a repeat experiment, fluoride (0·01 mole) (method as for silver chlorofluoroacetate, above).

The silver salt (3·3 g.) with bromine and chlorine (as for silver monofluoroacetate) gave (at 100°) dibromofluoromethane, b. p. 64·5° (64%) (Found: *M*, 191. Calc. for $CHBr_2F$: *M*, 192) (Swarts, *Bull. Acad. roy. Belg.*, 1910, **113**, reports b. p. 65°), and (at 40°) bromochlorofluoromethane (67%). Silver bromofluoroacetate (5·1 g.), mixed with a 300% excess of powdered iodine and heated at 1 mm., gave, after preliminary fractionation in a vacuum before distillation *in vacuo* through a micro-column, *bromofluoroiodomethane* (19%), b. p. 35°/70 mm. 102—104°/760 mm. (decomp.) (Found: C, 5·9; H, 0·4; F, 8·0; I, 52·9. CHBrFI requires C, 5·0; H, 0·4; F, 7·95; I, 53·1%), whose decomposition was accelerated by light and traces of moisture. This decomposition accounts for the poor analyses for carbon, a feature characteristic of some other similar compounds.

Fluoroiodoacetic Acid.—Prepared from ethyl bromofluoroacetate (see above) by Swarts's method (*Zentr.*, 1903, I, 13) (20% yield), this acid was converted into impure silver fluoroiodoacetate with some decomposition (Found: Ag, 38·2. Calc. for C_2HFIO_2Ag: Ag, 34·7%). The salts with excess of iodine (as for silver bromofluoroacetate) gave fluorodi-iodomethane (18% yield from fluoroiodoacetic acid), b. p. 50°/50 mm. (Found: F, 6·4; I, 87·9%; *M*, 278, 280. Calc. for CHI_2F: F, 6·6; I, 88·8%; *M*, 286). Ruff, Bretschneider, Luchsinger, and Miltschitzky (*Ber.*, 1936, **69**, 299) report b. p. 100°.

Difluoroacetic Acid.—This was prepared in 61% yield from tetrafluoroethylene by hydrolysis with sulphuric acid of ethyl 1 : 1 : 2 : 2-tetrafluoroethyl ether (b. p. 58°; obtained in 94% yield by reaction of tetrafluoroethylene with ethanol and sodium ethoxide). *Silver difluoroacetate* (91% yield from 15·1 g. of acid) (Found: Ag, 53·0. $C_2HO_2F_2Ag$ requires Ag, 53·2%) was prepared by the method given below for perfluoro-acids. Like silver trifluoroacetate, silver difluoroacetate is readily soluble in water, ether, and benzene. Silver difluoroacetate (3·2 g.) and dry chlorine (10% excess) at 50° in a steel bomb gave chlorodifluoromethane (91%), b. p. −41° (Found: *M*, 86. Calc. for $CHClF_2$: *M*, 86·5). Benning and McHarness (*Ind. Eng. Chem.*, 1940, **32**, 814) report b. p. −40·8°. The reaction also occurs readily (87% yield) at atmospheric pressure by condensing chlorine on to the silver salt (5·2 g.), allowing the mixture to warm to room temperature, and passing more chlorine into the solid while heating it gently with a free flame.

The silver salt (3·1 g.) and bromine (50% excess) at 50—60°, and finally at 100°, gave bromodifluoromethane (88%), b. p. −15° (Found: *M*, 131. Calc. for $CHBrF_2$: *M*, 131). Henne (*J. Amer. Chem. Soc.*, 1937, **59**, 1200) reports b. p. −14·5°. In an autoclave the yield was 93%, and required only a 5% excess of bromine. Silver difluoroacetate (10·1 g.), intimately mixed with powdered iodine (50% excess), was heated with a free flame under an air-condenser leading to traps cooled by liquid air. Smooth reaction occurred at *ca.* 150° to give carbon dioxide (98%) and difluoroiodomethane (93%), b. p. 20·5°, a colourless liquid liberating iodine on exposure to light (Found: C, 6·6; H, 0·5%; *M*, 178. Calc. for CHF_2I: C, 6·7; H, 0·7%; *M*, 178). Ruff (*Ber.*, 1936, **69**, 299) reports b. p. (calc.) 21·6°. When heated to 220° with mercury (2 ml.), difluoroiodomethane (4·0 g.) gave 1 : 1 : 2 : 2-tetrafluoroethane (40%) (Found: *M*, 102. Calc. for $C_2H_2F_4$: *M*, 102), silicon tetrafluoride, carbon dioxide, and hydrogen fluoride.

Bromochlorofluoroacetic Acid.—Bromofluoroacetyl chloride (73% yield from the acid) and excess of chlorine were exposed at 120° to ultra-violet light for 6 days. After dissolution in water the organic acids were extracted by ether and distilled from a trace of phosphoric oxide, to give bromochlorofluoroacetic acid (31%) and a trace of dichlorofluoroacetic acid (5%); no bromofluoroacetic acid was detected in the bromochlorofluoroacetic acid. With silver oxide and a trace of phosphoric oxide, bromochlorofluoroacetic acid gave *silver bromochlorofluoroacetate* (Found: Ag, 35·7. $C_2O_2BrClFAg$ requires Ag, 36·2%), 5 g. of which with bromine yielded *dibromochlorofluoromethane* (71%), b. p. 79·5—80·5° (Found: Br + Cl, 85·9; F, 8·4%; *M*, 224. CBr_2ClF requires Br + Cl, 86·3; F, 8·4%; *M*, 226·5). Chlorine similarly gave bromodichlorofluoromethane (see above) (63%).

Dichlorofluoroacetic Acid.—Chlorofluoroacetic acid (10·0 g.) was converted into *chlorofluoroacetyl chloride* (57%), b. p. 70—72° (Found: acyl Cl, 27·7; total Cl, 54·3%; *M*, 129; $CHOCl_2F$ requires acyl Cl, 27·1; total Cl, 54·2%; *M*, 131), which was mixed with a 20% excess of chlorine in a silica tube and exposed at 80° to intense ultra-violet radiation for 14 days. After dissolution in water, the organic acids were extracted by ether and distilled, to give a mixture of chloro- (48%) and dichloro-fluoroacetic acid (31%), b. p. 95°/28 mm. (yields determined by analysis for chlorine and titration). Reaction of the mixed silver salts (from 5·1 g. of mixed acid) with bromine by the method used for chlorofluoroacetic acid yielded bromochlorofluoromethane (61% based on the silver chlorofluoroacetate), b. p. 36—37°, and *bromodichlorofluoromethane* (58% based on the silver dichlorofluoroacetate), b. p. 51—52° (Found: C, 6·4%; *M*, 181. $CBrCl_2F$ requires C, 6·6%; *M*, 182). Chlorine similarly gave dichlorofluoromethane (78% based on silver chlorofluoroacetate) (see above) and trichlorofluoromethane, b. p. 23—24° (63% based on silver dichlorofluoroacetate) (Found: *M*, 136. Calc. for CCl_3F: *M*, 137·5). Benning and McHarness (*loc. cit.*) report b. p. 23·77°. An excess of iodine, heated with the mixture of silver salts (4·6 g.), gave chlorofluoroiodomethane (29% based on silver chlorofluoroacetate) (see above), *dichlorofluoroiodomethane* (10% based on silver dichlorofluoroacetate), b. p. 44—46°/210 mm. (Found: F, 8·2; I, 55·3. CCl_2IF requires F, 8·3; I, 55·5%), and a mixture of the fluorochloro-iodides (15%) which could not be separated by distillation on the scale used. Dichlorofluoroiodomethane liberated iodine rapidly when kept and gave tetrachloro-1 : 2-difluoroethane amongst the products. After 8 hours' heating at 150°, the yield of tetrachloro-1 : 2-difluoroethane was 41%.

Bromodifluoroacetic Acid.—This acid was prepared by Swarts's method (*Zentr.*, 1903, II, 710) (8% yield) and converted into *silver bromodifluoroacetate* (Found: Ag, 38·1. $C_2O_2BrF_2Ag$ requires Ag, 38·3%) which, with an excess of bromine, yielded dibromodifluoromethane (81%), b. p. 25° (Found: *M*, 210. Calc. for CBr_2F_2: *M*, 210). The reaction with an excess of iodine gave less than 5% of a compound (not definitely identified) believed to be bromodifluoroiodomethane.

Chlorodifluoroacetic Acid.—Prepared in 65% yield by permanganate oxidation of 1 : 1 : 2 : 3-tetrachloro-3 : 3-difluoropropene, this gave a *silver* salt (77%) (Found: Ag, 45·6. $C_2O_2ClF_2Ag$ requires Ag, 45·5%) by the method used for chlorofluoroacetic acid. The silver salt (0·02 mole) decomposed in water during 14 days, to give silver chloride (0·02 mole) and oxalic acid (0·019 mole); a second experiment gave fluoride (0·039 mole).

Reaction with chlorine and bromine as described for difluoroacetic acid gave, from 5 g. of silver salt, dichlorodifluoromethane (88%), b. p. −29·5° (Found: *M*, 121. Calc. for CCl_2F_2: *M*, 121) (Bichowsky and Gilbey, *Ind. Eng. Chem.*, 1931, **23**, 366, give b. p. −29·8°), and *bromochlorodifluoromethane* (91%), b. p. −4° (Found: C, 6·9; Br + Cl, 69·6; F, 22·7%; *M*, 165. $CBrClF_2$ requires C, 7·3; Br + Cl, 69·8; F, 23·0%; *M*, 165·5). Heating with iodine at a pressure of 10 mm., so that the product was removed from the reaction vessel as rapidly as

possible, gave *chlorodifluoroiodomethane* (78% from 10 g. of silver salt), b. p. 33° (Found: C, 5·6; Cl + I, 76·9%; *M*, 212. $CClF_2I$ requires C, 5·65; Cl + I, 76·5%; *M*, 212·5), purified by fractionation *in vacuo*. It liberated iodine rapidly on exposure to light and oxygen; when shaken with excess of mercury in a Pyrex tube exposed to ultra-violet light, chlorodifluoroiodomethane (2·1 g.) was converted into 1 : 2-dichlorotetrafluoroethane (81%) (Found: *M*, 171. Calc. for $C_2Cl_2F_4$: *M*, 171), whose structure was proved by dehalogenation with zinc and ethanol in a sealed tube at 80° to tetrafluoroethylene, identified spectroscopically. The yield of dichlorotetrafluoroethane obtained by heating the iodo-compound to 200° for 8 hours was 62%.

Chlorodifluoroiodomethane and chlorine or bromine in ultra-violet light give dichloro- (95%) or bromochloro-difluoromethane (94%).

Perfluoro-acids.—The following perfluoro-acids were prepared by the general method recorded in *Nature*, 1950, **166**, 192, and 1951, **168**, 1028, and *via* the corresponding perfluoroalkylmagnesium iodides (*ibid.*, 1951, **167**, 139; *J.*, 1952, 3423): pentafluoropropionic, heptafluoro-*n*-butyric, nonafluorovaleric, undecafluoro-*n*-hexanoic, tridecafluoro-*n*-heptanoic, and pentadecafluoro-*n*-octanoic acid. The *silver* salts (see Table) were prepared by addition of the acid (10 g.) to the theoretical amount of silver carbonate suspended in water (100 ml.). The soluble silver salts of the lower perfluoro-acids are obtained by evaporation of the aqueous solution to dryness under reduced pressure. The higher perfluoro-acids and their silver salts are much less soluble in water; complete reaction of the acids with silver carbonate was ensured by heating them at 60° for 30 minutes, and the silver salt was obtained by extraction of the suspended solid and of the aqueous solution with ether, followed by evaporation of the ethereal extracts. The salts

Salt	Yield	Ag, found, %	Ag, required, %	Salt	Yield	Ag, found, %	Ag, required, %
$C_3F_5{\cdot}CO_2Ag$ ...	95	39·7	39·9	$C_5F_{11}{\cdot}CO_2Ag$	93	25·6	25·7
$C_3F_7{\cdot}CO_2Ag$ ...	98	33·2	33·6	$C_6F_{13}{\cdot}CO_2Ag$	92	22·8	22·9
$C_4F_9{\cdot}CO_2Ag$ ...	96	29·1	29·1	$C_7F_{15}{\cdot}CO_2Ag$	94	20·5	20·7

are soluble in ether and crystallise from carbon tetrachloride or ether as greasy, pearly plates, which were dried *in vacuo* before use. Reaction of 0·01 mole with chlorine carried out (*a*) in a small stainless-steel autoclave at 50° (10% excess of chlorine), or (*b*) by passage of chlorine (20% excess) at atmospheric pressure through the vigorously stirred salt heated from 50° to 100°, gave the following: Chloropentafluoroethane (94%), b. p. −37° (Found: *M*, 154. Calc. for C_2ClF_5: *M*, 154·5) (Calfee, Fukuhara, Young, and Bigelow, *J. Amer. Chem. Soc.*, 1940, **62**, 267, report b. p. −38°). 1-*Chloroheptafluoropropane* (91%), b. p. −1° (Found: C, 17·7%; *M*, 204. C_3ClF_7 requires C, 17·6%; *M*, 204·5). 1-*Chlorononafluorobutane* (89%), b. p. 30° (Found: C, 18·5%; *M*, 253. C_4ClF_9 requires C, 18·9%; *M*, 254·5). 1-*Chloroundecafluoropentane* (85% from 0·005 mole), b. p. 60°, n_D^{10} 1·280 (Found: C, 19·3%; *M*, 303. C_5ClF_{11} requires C, 19·7%; *M*, 304·5). 1-*Chlorotridecafluorohexane* (83% from 0·005 mole), b. p. 86°, n_D^{15} 1·287 (Found: C, 20·2%; *M*, 352. C_6ClF_{13} requires C, 20·3%; *M*, 354·5). 1-*Chloropentadecafluoroheptane* (80% from 0·005 mole), b. p. 109°, n_D^{15} 1·292 (Found: C, 20·6%; *M*, 400, 405. C_7ClF_{15} requires C, 20·8%; *M*, 404·5).

Reaction with bromine, effected as in (*a*) above (for the less volatile fluoro-bromides), or by heating a thin layer of silver salt with a 30% excess of bromine, gave bromopentafluoroethane (98%), b. p. −20° (Found: *M*, 200. Calc. for C_2BrF_5: *M*, 199) (Brice, Pearlson, and Simons, *ibid.*, 1946, **68**, 968, report b. p. −23° to −21°), 1-bromoheptafluoropropane (97%), b. p. 12° (Found: *M*, 248. Calc. for C_3BrF_7: *M*, 249) (Brice *et al.*, *loc. cit.*, report b. p. 12° for a mixture of isomers), 1-*bromononafluorobutane* (95%), b. p. 44° (Found: C, 16·3%; *M*, 298. C_4BrF_9 requires C, 16·1%; *M*, 299), 1-*bromoundecafluoropentane* (91%), b. p. 74·5° (Found: C, 17·2%; *M*, 345. C_5BrF_{11} requires C, 17·2%; *M*, 349), 1-*bromotridecafluorohexane* (90% from 0·005 mole), b. p. 100° (Found: C, 17·7%; *M*, 393, 397. C_6BrF_{13} requires C, 18·0%; *M*, 399), and 1-*bromopentadecafluoroheptane* (86% from 0·005 mole), micro-b. p. 123—124° (Found: C, 18·7. C_7BrF_{15} requires C, 18·7%).

Fluoro-iodides were prepared from the silver salts by use of an autoclave or by heating with a free flame an intimate mixture of silver salt and powdered iodine (200% excess) (cf. Part I). The temperature of the reflux condenser and the pressure in the reaction flask (600 mm. to 2 mm.) were controlled so that the iodo-compound was removed rapidly. The by-products from the reactions will be discussed later. The products were pentafluoroiodoethane (94%), b. p. 13° (Found: *M*, 246. Calc. for C_2F_5I: *M*, 246) (Banks, Emeléus, Haszeldine, and Kerrigan, *J.*, 1948, 2188, report b. p. 13°), heptafluoroiodopropane (90%), b. p. 39·5° (Found: *M*, 296. Calc. for C_3F_7I: *M*, 296) (Haszeldine, *J.*, 1949, 2856; 1950, 2789, reports b. p. 39—

40°), *nonafluoro-1-iodobutane* (89%), b. p. 67° (Found: C, 13·5%; *M*, 345. C_4F_9I requires C, 13·9%; *M*, 346), *undecafluoro-1-iodopentane* (89%), b. p. 95°, n_D^{20} 1·320 (Found: C, 15·1%; *M*, 393. $C_5F_{11}I$ requires C, 15·2%; *M*, 396), *tridecafluoro-1-iodohexane* (90% from 0·005 mole), b. p. 117°, n_D^{20} 1·322 (Found: C, 16·2. $C_6F_{13}I$ requires C, 16·1%), and *pentadecafluoro-1-iodoheptane* (85% from 0·005 mole), b. p. 137—138°, n_D^{20} 1·323 (Found: C, 16·8. $C_7F_{15}I$ requires C, 16·9%).

Reactions with Alcoholic Potassium Hydroxide.—One-g. samples of the following compounds were completely destroyed by 15 ml. of potassium hydroxide solution (15% in 95% ethanol) after 48 hours at 35°, to give (*a*) fluoride and halide: CH_2IF, CH_2BrF, CH_2ClF, (*b*) fluoride, halide, and formate: $CHClIF$, $CHCl_2F$, $CHClBrF$, CHI_2F, or (*c*) fluoride, halide, and carbonate: $CClBrIF$, $CClBr_2F$, CCl_2BrF, CCl_2IF. Under similar conditions $CHClF_2$ and CH_2F_2 were stable, and $CClIF_2$ and $CHIF_2$ yielded $CHClF_2$ (24%) and CH_2F_2 (19%) and halide and carbonate. Heptafluoroiodopropane (5·0 g.), with alcoholic potassium hydroxide at 100°, gave heptafluoropropane (70%), ethyl 1 : 1 : 2 : 3 : 3 : 3-hexafluoropropyl ether (5%) (identical with the ether prepared by the sodium ethoxide-catalysed reaction of ethanol with hexafluoropropene), and fluoride (15%).

Miscellaneous Reactions with Silver Trifluoroacetate.—(a) *With phosphorus.* Silver trifluoroacetate (4·0 g.), heated to 180° for 12 hours with an excess of yellow phosphorus (6 g.; freed from the oxide by dipping into carbon disulphide), gave silver phosphide, a trace of carbon dioxide, and trifluoroacetic anhydride (61%), b. p. 40° (Found: *M*, 209. Calc. for $C_4F_6O_3$: *M*, 210), which dissolved in aqueous sodium hydroxide without evolution of fluoroform. (Tristrifluoromethylphosphine would have given fluoroform.) A similar reaction at 310° for 12 hours gave trifluoroacetic anhydride (67%) identified as above, and *ca.* 5% of carbon dioxide and silicon tetrafluoride. (b) *With sulphur.* Silver trifluoroacetate (3·0 g.), mixed with an excess of sulphur (7 g.) and heated at 300° for 12 hours, gave silver sulphide, trifluoroacetic anhydride (81%), b. p. 40° (*M*, 210), which dissolved completely in water, subsequently made alkaline without liberation of fluoroform or fluoride, and sulphur dioxide (84%), b. p. −10° (*M*, 64). (Bistrifluoromethyl sulphide is stable to water and base; bistrifluoromethyl disulphide gives fluoride with base.) (c) *With mercury.* In a single experiment, mercury was heated with silver trifluoroacetate at 300° for 12 hours, giving carbonyl fluoride and silicon tetrafluoride, but not bistrifluoromethylmercury. (d) *With arsenic and phosphorus iodides.* Single attempts to prepare trifluoromethyl-arsines or -phosphines in good yield by the reaction of the silver salt, arsenic or phosphorus, and iodine were unsuccessful.

Reactions of Trifluoroacetic Anhydride and Trifluoroacetyl Chloride with Halogens.—Trifluoroacetic anhydride (3·0 g.) with an excess of iodine (12 g.) at 350° for 12 hours gave carbon monoxide, carbon dioxide, and trifluoroiodomethane (63%), b. p. −22° (Found: *M*, 196. Calc. for CIF_3: *M*, 196).

Trifluoroacetyl chloride (2·2 g.) was heated with an excess of chlorine at 280° for 7 hours; the volatile products were completely absorbed by aqueous sodium hydroxide (to which chlorotrifluoromethane is stable). An experiment with bromine at 340° for 12 hours gave a similar result.

Reaction of Sodium Heptafluorobutyrate and Pentafluoropropionate with Bromine or Iodine.—The reaction of bromine (300% excess) with dried sodium heptafluorobutyrate (10·0 g.), heated strongly with a free flame, was slow and much of the bromine distilled through the reflux condenser and was trapped in liquid-air traps. The products were 1-bromoheptafluoropropane (18%) (Found: *M*, 249. Calc. for C_3BrF_7: *M*, 249) and 1 : 2-dibromohexafluoropropane (27%), b. p. 71° (Found: C, 11·5%; *M*, 310. Calc. for $C_3Br_2F_6$: C, 11·6%; *M*, 310), identified by infra-red spectroscopy. Reaction in an autoclave at 260° for 12 hours gave 32% of bromoheptafluoropropane and 34% of dibromohexafluoropropane. Reaction with iodine at atmospheric pressure similarly gave heptafluoroiodopropane (9%), b. p. 39—40° (Found: *M*, 296. Calc. for C_3IF_7: *M*, 296), and hexafluoropropene (41%), b. p. −29° (Found: *M*, 150. Calc. for C_3F_6: *M*, 150), identified by comparison of its infra-red spectrum with that of a known specimen. In an autoclave at 250° for 4 hours the yields were 5% and 37%.

Sodium pentafluoropropionate (3·0 g.), heated with an excess of bromine in a small autoclave at 260° for 8 hours, gave bromopentafluoropropane (8%) and 1 : 2-dibromotetrafluoroethane (43%), b. p. 45—47° (Found: *M*, 258. Calc. for $C_2Br_2F_4$: *M*, 260), whose identity was confirmed by its infra-red spectrum. Iodine similarly yielded pentafluoroiodoethane (7%), 1 : 2-di-iodotetrafluoroethane (35%), b. p. 112° (Emeléus and Haszeldine, *loc. cit.*, report b. p. 112°), and perfluoro*cyclo*butane (13%), b. p. *ca.* −2° (Found: *M*, 200. Calc. for C_4F_8: *M*, 200).

Thermal Decomposition of Sodium Salts of Perfluoro-acids.—Sodium heptafluorobutyrate.

The salt (8·7 g.) was spread evenly down a horizontal silica tube (2 cm. in diameter), closed at one end, with the other end leading *via* two traps cooled by liquid air to an oil-pump. The pressure in the tube was reduced to 50 mm., maintained by a manostat, and the silica tube was slowly moved into a furnace heated to 280°. Steady evolution of gas occurred and the rate of reaction was controlled by the speed of movement into the furnace. The temperature of the furnace was finally raised to 320°. The condensed products were carbon dioxide and hexafluoropropene (92%), b. p. −29° (Found: *M*, 150. Calc. for C_3F_6: *M*, 150), identified by its infra-red spectrum. A second experiment, carried out at atmospheric pressure in nitrogen, gave a 90% yield of olefin. The reaction is slow at 200—220°, but is rapid and essentially quantitative at 230—280°. The residue in the reaction tube (which need not be of silica) was sodium fluoride. Decarboxylation can be effected by a free flame or oil-bath, but the yields are lower (75—85%), and temperature control is advisable.

Sodium pentafluoropropionate (5·7 g.) at 270°/150 mm. yielded tetrafluoroethylene (84%) (Found: *M*, 100. Calc. for C_2F_4: *M*, 100) and perfluoro*cyclo*butane (4%) (Found: *M*, 200. Calc. for C_4F_8: *M*, 200), identified spectroscopically.

Sodium nonafluorovalerate (3·7 g.) was converted, at 290°/100 mm., into *octafluorobut*-1-*ene* (77%), b. p. 0·8° (Found: C, 23·8%; *M*, 200. C_4F_8 requires C, 24·0%; *M*, 200), distinguished from its isomeric perfluoro*cyclo*butane and octafluorobut-2-ene by its infra-red spectrum and particularly the band at 5·56 μ. Miller *et al.* (*Ind. Eng. Chem.*, 1947, **39**, 333, 401) report the preparation of octafluorobut-1-ene, but give no physical properties. Minnesota Mining and Manufacturing Co. report b. p. −2° to −1° at 730 mm. (personal communication). Permanganate oxidation of octafluorobut-1-ene yielded pentafluoropropionic acid (56%), characterised as its amide.

Sodium tridecafluoro-*n*-heptanoate (3·3 g.) similarly gave *dodecafluorohex*-1-*ene* (65%), b. p. 57° (Found: C, 24·1%; *M*, 297. C_6F_{12} requires C, 24·0%; *M*, 300), showing absorption at 5·56 μ. Permanganate oxidation gave nonafluorovaleric acid (52%).

Sodium pentadecafluoro-octanoate (3·8 g.) yielded *tetradecafluorohept*-1-*ene* (60%), b. p. 82—83° (Found: C, 23·7%; *M*, 348. C_7F_{14} requires C, 24·0%; *M*, 350), showing strong absorption at 5·56 μ. Permanganate oxidation yielded undecafluorohexanoic acid (49%).

Sodium heptadecafluorononanoate (2·2 g.) at 300°/5 mm. gave *hexadecafluoro-oct*-1-*ene* (47%), micro-b. p. 105° (Found: C, 23·9%; *M*, 392, 396. C_8F_{16} requires C, 24·0%; *M*, 400), oxidised by permanganate to tridecafluoro-*n*-heptanoic acid (61%). Oxidation of this and the other olefins described above was effected by treatment at 100—130° with a 20% excess of alkaline potassium permanganate in a 100-ml. autoclave. The aqueous solution was treated with sulphur dioxide, acidified with sulphuric acid and extracted with ether in the usual way. After removal of the ether through a Vigreux column, the residual acid was distilled or recrystallised from carbon tetrachloride.

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818. *The Synthesis of 2-Imino-3-phenyl- and -3 : 3-diphenyl-pyrrolidines.*

By F. E. KING, K. G. LATHAM, and M. W. PARTRIDGE.

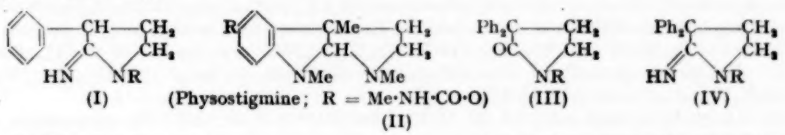
Under conditions appropriate to the formation of amidines, 3-halogeno-1-phenyl- and -1 : 1-diphenyl-propyl cyanides have been converted into 2-iminopyrrolidines.

2-IMINO-3-PHENYLPYRROLIDINES, *e.g.*, (I), possess certain structural features of the physostigmine (eserine) ring-system (II) and for that reason appeared to merit pharmacological examination; moreover Blicke and Zambito (Abstr. 111th Meeting Amer. Chem. Soc., April 1947, p. 3K) have reported that the somewhat related 1-ethyl-3 : 3-diphenyl-2-pyrrolidone (III; R = Et) has decided analgesic activity. The preparation of compounds of type (I) and of the analogous 2-imino-3 : 3-diphenylpyrrolidines (IV) was therefore undertaken, starting from 3-halogeno-1-phenyl- and -1 : 1-diphenyl-propyl cyanides as follows.

The monophenyl-cyanide (V) was readily converted into the hydrochloride of the imino-ether (VI), but treatment with ammonia gave, not the corresponding amidine, but

the hydrochloride of 2-imino-3-phenylpyrrolidine (I; R = H), which amine was also formed when the chloro-cyanide (V) was heated with alcoholic ammonia. Heating the cyanide (V) with aniline benzenesulphonate and even with aniline gave the *N*-phenyl base (I; R = Ph). This imino-pyrrolidone was hydrolysed by nitrous acid to the related 1 : 3-diphenylpyrrolidone, a reaction which excludes the alternative 3-phenyl-2-phenyliminopyrrolidine structure.

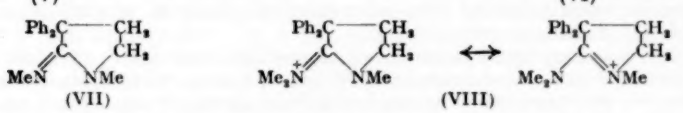
Although Blicke and Zambito (*loc. cit.*) presume the intermediate formation of an imino-ether salt in converting 3-diethylamino-1 : 1-diphenylpropyl cyanide into 1-ethyl-2-imino-3 : 3-diphenylpyrrolidine (IV; R = Et), we were unable to prepare imino-ethers from either 3-chloro- or 3-bromo-1 : 1-diphenylpropyl cyanide (Pinner conditions, 44 days). However, when the bromo-cyanide was heated with aniline or aniline benzenesulphonate, 2-imino-1 : 3 : 3-triphenylpyrrolidine (IV; R = Ph) was obtained, the assigned constitution being sustained by hydrolysis of the base with nitrous acid to 1 : 3 : 3-triphenyl-2-pyrrolidone (III; R = Ph).



(I) (Physostigmine; R = Me·NH·CO·O) (II) (III) (IV)

NC·CHPh·CH_2·CH_2Cl (V)

EtO·C(:NH)·CHPh·CH_2·CH_2Cl,HCl (VI)



(VII) (VIII)

In a later personal communication from Professor Blicke, heating in a stream of hydrogen chloride is given as a method by which the diethylamino-cyanide is cyclised to the imino-pyrrolidine (IV; R = Et).

The action of methylamine on 3-bromo-1 : 1-diphenylpropyl cyanide produced a mixture of 2-imino-1-methyl-3 : 3-diphenylpyrrolidine (IV; R = Me) and 1-methyl-2-methylimino-3 : 3-diphenylpyrrolidine (VII), separated by crystallisation of the picrates. The existence of the iminopyrrolidine (IV; R = Me) has been postulated by Morrison and Rinderknecht (*J.*, 1950, 1478) but the compound was not characterised. The reaction leading to the production of (VII) is indicated by the formation of the ditertiary base when the monomethyl compound (IV; R = Me) was heated with excess of methylamine. Similarly, the action of methyl iodide on (IV; R = Me) gives the tertiary base (VII); excess of the reagent on both (IV; R = Me) and (VII) afforded the identical quaternary product isolated in the form of a methopicrate. This is unquestionably the 2-*N*-dimethyl compound for the cation of which the resonance structure (VIII) can be postulated.

Biological tests were carried out through the kindness of Dr. G. E. Ullyot of the Smith, Kline, and French Laboratories, Philadelphia. They show that the iminopyrrolidines (I; R = Ph), (IV; R = Me), (IV; R = Ph), and (VII) fail to antagonise leptazol(metrazol)-induced convulsions in mice, and that (IV; R = Me) and (VII) are without analgesic activity.

Experimental

3-Hydroxy-1-phenylpropyl Cyanide.—The preparation of 3-hydroxyl-1-phenylpropyl cyanide due to Knowles and Cloke (*J. Amer. Chem. Soc.*, 1932, **54**, 2028) was found unsatisfactory (yields 22%) and has even been reported to fail completely (Anker and Cook, *J.*, 1948, 806). The following modification affords consistent yields of *ca.* 50%.

Sodamide (40 g., 2 mols.), powdered in a ball-mill and dispersed in benzene (80 c.c.) and ether (300 c.c.), was slowly treated with benzyl cyanide (60 g.), and the mixture heated under reflux for 2 hours. Ethylene chlorohydrin (41 g., 1 mol.) was then added at 0° during 2 hours and next day the mixture was shaken with water. 3-Hydroxy-1-phenyl cyanide was isolated from the dried organic solution by distillation and had b. p. 141—145°/1—1·2 mm., n_D^{21} 1·5409, d_4^{20} 1·0587, $[R_L]_D$ 46·21 (calc. 46·28).

A solution in ether with *p*-nitrobenzoyl chloride and 2N-sodium hydroxide gave the p-*nitrobenzoyl* ester which crystallised from methanol in prisms, m. p. 76° (Found: N, 9·0. $C_{17}H_{14}O_4N_2$ requires N, 9·0%). The *toluene*-p-*sulphonate*, similarly prepared, was an oil, b. p. 142—150°/2 mm. (Found: N, 4·7. $C_{17}H_{17}O_3NS$ requires N, 4·4%).

4-*Chloro*-1-*ethoxy*-1-*imino*-2-*phenylbutane Hydrochloride* (VI).—A mixture of 3-chloro-1-phenylpropyl cyanide (27 g.), prepared from the foregoing hydroxy-cyanide by the method of Anker and Cook (*loc. cit.*), and ethanol (7 g.) was treated with hydrogen chloride (6·6 g., 1·2 mols.) at 0° and kept at that temperature for 5 days. The *imino-ether hydrochloride* (28·3 g., 72%) then precipitated by dry ether formed prisms, m. p. 96° (Found: N, 5·5. $C_{12}H_{16}ONCl,HCl$ requires N, 5·3%). Treatment with sodium picrate in ice-cold aqueous solution gave the *picrate* which crystallised from ethanol as yellow needles, m. p. 127—128° (Found: N, 12·6 $C_{12}H_{16}ONCl,C_6H_3O_7N_3$ requires N, 12·3%).

2-*Imino*-3-*phenylpyrrolidine* (I; R = H).—(i) A solution of 4-chloro-1-ethoxy-1-imino-2-phenylbutane hydrochloride (28·3 g.) in 10% ethanolic ammonia (270 c.c., 18 mols.) was set aside at room temperature for 5 days. It was then concentrated to precipitate ammonium chloride, 2-*imino*-3-*phenylpyrrolidine hydrochloride* (11·4 g., 54%) being obtained by evaporation of the filtrate and crystallisation of the residue from *iso*propanol as hygroscopic prisms, m. p. 186° (Found: C, 60·8; H, 6·7; N, 14·7. $C_{10}H_{12}N_2,HCl$ requires C, 61·0; H, 6·8; N, 14·2%). The *picrate* crystallised from ethanol in yellow needles, m. p. 195° (Found: N, 17·7. $C_{10}H_{12}N_2,C_6H_3O_7N_3$ requires N, 18·0%).

With sodium hydroxide solution the hydrochloride gave 2-*imino*-3-*phenylpyrrolidine* which was collected in chloroform and crystallised from carbon tetrachloride in rods, m. p. 93° (Found: N, 17·4. $C_{10}H_{12}N_2$ requires N, 17·5%). Treated with benzenesulphonic acid it afforded the *benzenesulphonate* which separated from *iso*propanol in prisms, m. p. 147° (Found: N, 8·8. $C_{10}H_{12}N_2,C_6H_6O_3S$ requires N, 8·8%).

(ii) 3-Chloro-1-phenylpropyl cyanide (18 g.), ammonium chloride (0·1 g.), and 8·7% ethanolic ammonia (60 c.c., 3 mols.) were heated at 130° for 90 hours. Ammonium chloride (2·65 g.) was collected and the concentrated filtrate basified and extracted with chloroform. The base was isolated as the picrate which when recrystallised from ethanol was obtained as needles (7·8 g., 20%), m. p. and mixed m. p. 195°.

2-*Imino*-1 : 3-*diphenylpyrrolidine* (I; R = Ph).—(i) 3-Chloro-1-phenylpropyl cyanide (6·3 g.) and aniline benzenesulphonate (8·8 g., 1 mol.) were heated at 210° until hydrogen chloride evolution had almost ceased (*ca.* 1¾ hours). The product was dissolved in hot *iso*propanol (50 c.c.) and light petroleum (b. p. 80—100°) (20 c.c.); recrystallisation of the solid (9·4 g., 68%), m. p. 136—140°, which separated in the cold afforded 2-*imino*-1 : 3-*diphenylpyrrolidine benzenesulphonate* as plates, m. p. 147—149° (Found: N, 6·7. $C_{22}H_{22}O_3N_2S$ requires N, 7·1%).

Treatment of the residual *iso*propanol–petroleum solution with aqueous sodium hydroxide gave additional product as the free *base*, which separated from light petroleum in plates, m. p. 98° (Found: C, 80·8; H, 6·7; N, 11·9. $C_{16}H_{16}N_2$ requires C, 81·3; H, 6·8; N, 11·9%). 2-*Imino*-1 : 3-*diphenylpyrrolidine picrate* crystallised from ethanol in yellow rods, m. p. 222—223° (Found: N, 15·0. $C_{16}H_{16}N_2,C_6H_3O_7N_3$ requires N, 15·0%).

(ii) When the solid obtained by heating a mixture of 3-chloro-1-phenylpropyl cyanide (2·6 g.) and aniline (1·3 g., 1 mol.) at 185° for 2½ hours was dissolved in water, 2-imino-1 : 3-diphenylpyrrolidine (1·5 g., 44%) was obtained by the addition of sodium hydroxide. The crystallised product and its benzenesulphonate and picrate had the above recorded m. p.s and mixed m. p.s.

1 : 3-*Diphenyl*-2-*pyrrolidone*.—Mixed solutions of 2-imino-1 : 3-diphenylpyrrolidine (2·4 g.) in 2N-hydrochloric acid (5 c.c., 1 mol.) and of sodium nitrite (3·5 g., 5 mols.) in water (15 c.c.) were heated to 80—83° with the dropwise addition of 2N-hydrochloric acid (30 c.c., 6 mols.). The brown solid (1·3 g., 53%) which had separated after cooling was crystallised from light petroleum and then aqueous ethanol, 1 : 3-*diphenyl*-2-*pyrrolidone* thus being obtained as silky needles, m. p. 81—82° (Found: C, 80·6; H, 6·6; N, 6·2. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·4; N, 5·9%).

2-*Imino*-1 : 3 : 3-*triphenylpyrrolidine* (IV; R = Ph).—(i) 3-Bromo-1 : 1-diphenylpropyl cyanide (5 g.) and aniline benzenesulphonate (4·2 g., 1 mol.) were mixed and heated at 210° for 3¼ hours. Extraction with water left unchanged bromo-cyanide (2·4 g., 48%), and treatment of the solution with aqueous sodium hydroxide gave 2-*imino*-1 : 3 : 3-*triphenylpyrrolidine* (1·75 g., 34%) which crystallised from *iso*propanol in plates, m. p. 128° (Found: N, 8·9. $C_{22}H_{20}N_2$ requires N, 9·0%). The *picrate* formed orange-yellow prisms (from ethanol), m. p. 206—208° (Found: N, 12·8. $C_{22}H_{20}N_2,C_6H_3O_7N_3$ requires N, 12·9%).

(ii) The action of aniline (1 mol.) on 3-bromo-1 : 1-diphenylpropyl cyanide (1 mol.) at 185° for 2½ hours gave the foregoing pyrrolidine (61%), m. p. and mixed m. p. 128°.

1 : 3 : 3-*Triphenyl-2-pyrrolidone* (III; R = Ph).—Treatment of 2-imino-1 : 3 : 3-triphenylpyrrolidine (1·55 g.) with nitrous acid as described for the preparation of 1 : 3-diphenyl-2-pyrrolidone gave 1 : 3 : 3-*triphenyl-2-pyrrolidone* (1·5 g., 97%) which crystallised from ethanol in plates, m. p. 117—118° (Found: N, 4·6. $C_{22}H_{19}ON$ requires N, 4·5%).

1-*Methyl-2-methylimino-3* : 3-*diphenylpyrrolidine* (VII).—(i) 3-Bromo-1 : 1-diphenylpropyl cyanide (60 g.) (Bockmühl and Ehrhart, *Annalen*, 1948, **561**, 52), methylamine (39·3 g., 6·5 mols.), and ethanol (35 c.c.) were heated under pressure at 100° for 13 hours. The residue left on evaporation was treated with 2N-sodium hydroxide (130 c.c.), the mixed amines were extracted with chloroform, and the solution was dried and heated to remove solvent and residual methylamine. Fractionation of the hydrochlorides obtained by treatment in ethereal solution with hydrogen chloride failed to separate the products, but crystallisation of the picrates (83 g.), m. p. 135—139°, from ethanol gave the less soluble 1-*methyl-2-methylimino-3* : 3-*diphenylpyrrolidine picrate* (18·5 g., 19%) as yellow rods, m. p. 180—182° (Found: C, 58·7; H, 4·6; N, 14·3. $C_{18}H_{20}N_2,C_6H_3O_7N_3$ requires C, 58·4; H, 4·7; N, 14·2%). 1-*Methyl-2-methylimino-3* : 3-*diphenylpyrrolidine*, liberated from the picrate by lithium hydroxide (cf. Burger, *J. Amer. Chem. Soc.*, 1945, **67**, 1615) and collected in chloroform, crystallised from aqueous methanol in needles, m. p. 106° (Found: C, 81·5; H, 7·5; N, 10·7. $C_{18}H_{20}N_2$ requires C, 81·8; H, 7·6; N, 10·6%). The *hydrochloride* separated from *iso*propanol in long prisms, m. p. 292—293° (decomp.) (Found: C, 70·5; H, 6·8; H, 9·7. $C_{18}H_{20}N_2,HCl$ requires C, 72·0; H, 7·0; N, 9·3%). The *picrolonate*, prepared in methanol, formed yellow prisms, m. p. 216° (Found: C, 63·4; H, 5·4; N, 16·2. $C_{18}H_{20}N_2,C_{10}H_8O_5N_4$ requires C, 63·6; H, 5·3; N, 15·9%).

(ii) 2-Imino-1-methyl-3 : 3-diphenylpyrrolidine (from 5 g. of the picrate) was heated under pressure at 105° with methyl iodide (2 g., 1 mol.) and acetone (2 c.c.) for 15 hours. The brown crystalline product (2 g.), m. p. 238—248°, was shaken with chloroform and 2N-sodium hydroxide, and the chloroform solution evaporated, whereupon the residue gave 1-methyl-2-methylimino-3 : 3-diphenylpyrrolidine picrate (16%), m. p. and mixed m. p. 181—182°.

(iii) 2-Imino-1-methyl-3 : 3-diphenylpyrrolidine, from the picrate (1 g.), was heated with 33% alcoholic methylamine (5 c.c.) and methylamine hydrochloride (0·05 g.) in ethanol (5 c.c.) at 105° for 4 days. After evaporation of volatile substances the product gave a picrate (27%), m. p. 180—181° alone or mixed with 1-methyl-2-methylimino-3 : 3-diphenylpyrrolidine picrate.

2-*Imino-1-methyl-3* : 3-*diphenylpyrrolidine* (IV; R = Me).—The alcoholic solution from which 1-methyl-2-methylimino-3 : 3-diphenylpyrrolidine picrate was originally isolated contained the more soluble *picrate* of 2-imino-1-methyl-3 : 3-diphenylpyrrolidine which crystallised in clusters of orange prisms (14·1 g., 15%), m. p. 147—149° (Found: C, 57·6; H, 4·4; N, 14·6. $C_{17}H_{18}N_2,C_6H_3O_7N_3$ requires C, 57·6; H, 4·4; N, 14·6%). The free base obtained by treatment with lithium hydroxide failed to solidify. The *hydrochloride* crystallised from *iso*propanol in prisms, m. p. 224—225° (Found, in sample dried at 130° in a vacuum: C, 70·9; H, 7·4; N, 9·3. $C_{17}H_{18}N_2,HCl$ requires C, 71·2; H, 6·7; N, 9·8%), and the *picrolonate* from ethanol in yellow prisms, m. p. 189° (Found: C, 63·0; H, 4·8; N, 16·0. $C_{17}H_{18}N_2,C_{10}H_8O_5N_4$ requires C, 63·0; H, 5·1; N, 16·3%). A solution of the pyrrolidine in hydrochloric acid treated with sodium nitrite (5 mols.) on a steam-bath gave 1-methyl-3 : 3-diphenyl-2-pyrrolidone (57%), m. p. 145° (Dupré, Elks, Hems, Speyer, and Evans, *J.*, 1949, 500, record m. p. 146·5—147°) (Found: N, 5·4. Calc. for $C_{17}H_{17}ON$: N, 5·6%); 33% of the original pyrrolidine was recovered.

1-*Methyl-2-methylimino-3* : 3-*diphenylpyrrolidine Methopicrate*.—(i) 2-Imino-1-methyl-3 : 3-diphenylpyrrolidine was heated under reflux with potassium carbonate and excess of methyl iodide in acetone solution for several hours. The acetone was then distilled and the residue shaken with 2N-sodium hydroxide and chloroform. The product obtained from evaporation of the chloroform solution was dissolved in warm aqueous lactic acid (20%) and mixed with a solution of sodium picrate in water, thus causing the precipitation of 1-*methyl-2-methylimino-3* : 3-*diphenylpyrrolidine methopicrate* which crystallised from ethanol in orange plates (67%), m. p. 188° (Found: C, 59·5; H, 4·8; N, 13·8. $C_{25}H_{25}O_7N_5$ requires C, 59·2; H, 5·0; N, 13·9%). (ii) When 1-methyl-2-methylimino-3 : 3-diphenylpyrrolidine was heated under reflux with methyl iodide (1 mol.) the methopicrate (yield 65%) obtained from the product had m. p. 188° alone or mixed with the sample derived from the 2-imino-1-methylpyrrolidine.

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819. *Infra-red Spectrum of Nitric and of Deuteronitric Acid Vapour. Completion of Identification of the Fundamental Frequencies. Entropy of Nitric Acid. Barrier Resisting Rotation of the Hydroxyl Group.*

By (the late) HENRY COHN, C. K. INGOLD, and H. G. POOLE.

The infra-red spectra from 3700 to 440 cm.$^{-1}$ of nitric and deuteronitric acid as vapour are recorded and interpreted. Those fundamental frequencies which previous study of the Raman spectra of these acids had left unknown or doubtful have been found and identified, and those assignments of previously observed frequencies which had remained dubious have been settled. The derivation of thermodynamic quantities is illustrated by a calculation of the entropy of nitric acid, which agrees well with the calorimetric value.

The barrier resisting rotation of the hydroxyl or deuteroxyl group about the NO bond in the gaseous molecules is computed, from the torsional frequencies and entropy, to be in the neighbourhood of 10 kcal./mole. This large value is ascribed to internal hydrogen-bonding in the gas molecules. The frequency differences between vapours and liquids can be understood to result from intermolecular hydrogen-bonding in the liquid acids.

THE Raman spectrum of nitric acid has been recorded by many observers. These investigations have recently been reviewed and discussed (Ingold and Millen, *J.*, 1950, 2612). Most of the fundamental frequencies of the nitric acid molecule can be identified in the Raman spectrum, but not all of them. Consequently the spectroscopic information thus secured is insufficient to permit a satisfactory calculation of thermodynamic properties of nitric acid, such as the entropy.

All those fundamental frequencies which are too weak to be observed, or easily observed, in the Raman spectrum of nitric acid, are included among those which are expected to appear strongly in the infra-red spectrum. As only one investigation, moreover one made in somewhat difficult experimental conditions, of the infra-red spectrum has yet been recorded (Freymann and Freymann, *Compt. rend.*, 1946, **222**, 1339), the present re-examination of the spectrum was undertaken with the object of securing a complete account of the fundamental frequencies of nitric acid, and thus of providing a means for the evaluation of its thermodynamic properties.

The known Raman spectra are those of liquid nitric acid and liquid deuteronitric acid. We record below the infra-red spectra of nitric acid and deuteronitric acid, each in the form of vapour, as observed on a prism spectrometer over the spectral range 3700—440 cm.$^{-1}$

For purposes of interpretation, we have to take account of the geometry of the nitric acid molecule. Our most direct knowledge of the geometry of the gaseous molecule is that given by its electron-diffraction pattern (Maxwell and Moseley, *J. Chem. Phys.*, 1940, **8**, 742), and summarised in Fig. 1. The position of the hydrogen atom is not determined. Owing to its relative lightness, its exact position is not particularly critical for our conclusions; and therefore, for the purpose of making calculations, we have assigned it an arbitrary position, as indicated in Fig. 1, taking the OH bond-length to be that in water, 0·96 Å, and giving the NOH angle its "theoretical" value, 90°. The angle within the NO_2 group is only approximately determined by the diffraction pattern. Its value is somewhat critical for certain of our conclusions, and we shall later give reason for thinking that, the other dimensions being accepted, 135° would be a better estimate of this angle than 130°.

A recent *X*-ray investigation of the crystal structure of nitric acid has yielded approximate dimensions of the crystal molecule (Luzzati, *Acta Cryst.*, 1951, **4**, 120). The *X*-ray length of the N–(OH) bond is markedly smaller (1·30 ± 0·05 Å) than the electron-diffraction length, while the other geometrical parameters are the same to within the rather wide limits of uncertainty. The difference in the measured N–(OH) lengths may well reflect a real change of molecular form between the gas and the crystal, where, owing to inter-

molecular hydrogen-bonding, the NO_3 group would probably assume a shape somewhat more like that of the nitrate ion, which has three equal NO bonds. Accordingly, we have preferred to use the electron-diffraction values, in our discussion of the infra-red spectra of gaseous nitric and deuteronitric acid.

Nitric acid, as a penta-atomic molecule, has nine normal modes of vibration. But the hydrogen atom is so much lighter than the other atoms that these vibrations divide themselves fairly sharply into two sets.

In the first set, the OH group will move essentially as a single-atomic unit, the oxygen atom carrying its hydrogen atom with it. As to these vibrations, essentially vibrations of the NO_3 group, the molecule can be represented approximately by a tetra-atomic model, O_2NO', where O', an imaginary atom of mass 17, does duty for the hydroxyl group. There are accordingly six of these vibrations: they are approximately described by the first six drawings in Fig. 2. They can be regarded as derived from the known vibrations of the nitrate ion, which, as a trigonal tetra-atomic molecule, has four fundamental frequencies, but with two degenerate, splitting each into two, so that the total of four becomes six, as soon as one oxygen atom becomes differentiated from the others. The six vibrations can be approximately described, three as stretching, and two as bending vibrations, and one as an out-of-plane deformation. By assuming the symmetry C_{2v}, with the NO' bond, representing the N–(OH) bond, as the two-fold axis (hereafter called the C_{2v} axis), the

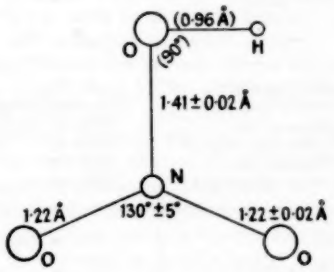


FIG. 1. *Model of the nitric acid molecule.*

(The geometrical parameters are as determined by Maxwell and Moseley, except those in parentheses, which are assumed.)

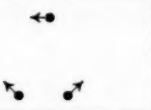
vibrations can be given an alternative approximate description: two stretching and one bending vibration are totally symmetrical (A_1) with respect to the assumed symmetry, one stretching and one bending vibration are non-totally symmetrical but planar (B_2), while the one out-of-plane vibration stands alone in its symmetry class (B_1). The corresponding six vibrations of deuteronitric acid could be similarly represented by the model O_2NO', where O' now has mass 18. Obviously the isotopic change will not greatly affect the frequencies of any of these vibrations.

In the second set of vibrations of nitric acid, nearly all the motion will be in the hydrogen atom, the NO_3 group remaining nearly rigid. There will be three of these vibrations, corresponding to the three degrees of freedom of motion of the hydrogen atom, as indicated in the last three drawings of Fig. 2. These vibrations can be approximately described as the stretching, bending, and twisting vibrations of the hydrogen atom. Under the symmetry C_s of the model of Fig. 1, the stretching and bending vibrations of hydrogen belong to the planar class (A'), while the twisting vibration belongs to the out-of-plane class (A'') of vibrations. The corresponding vibrations of deuteronitric acid will be similar, most of the motion being in the deuterium atom. Hence the isotopic change will strongly alter the frequencies of these vibrations.

The drawings of Fig. 2 are labelled in accordance with Redlich and Nielsen's scheme of numbering of the vibrations of nitric acid (*J. Amer. Chem. Soc.*, 1943, **65**, 654). In closer approximation than Fig. 2 describes, the two planar hydrogen C_s vibrations, nos. 7 and 8, belonging to class A', can mix, in principle at least, with the five planar C_{2v} vibrations nos. 1—5, of classes A_1 and B_2, which classes are to this extent not quite sharply separated from each other; while the out-of-plane hydrogen C_s vibration, no. 9, belonging to class A'', can mix with the out-of-plane C_{2v} vibration, no. 6, of class B_1. But in practice the relative

lightness of the hydrogen atom will militate against such mixings, as also will the outstandingly high value of the frequency of the hydrogen stretching vibration, no. 7, and the outstandingly low value of the frequency of the hydrogen twisting vibration, no. 9. It is the hydrogen-bending vibration, no. 8, of medium frequency, which is susceptible of most

FIG. 2. *Normal vibrations and observed frequencies (cm.$^{-1}$) of nitric acid.*

O_2NO' model [1]			
No. and C_{2v} class Description	1. (A_1) NO_2-stretching	2. (A_1) NO′-stretching	3. (A_1) NO_2-bending
HNO_3 Raman (liq.) [3]	1300 (*s*, *p*)	925 (*s*, *p*)	680 (*m*, *p*)
HNO_3 Infra-red (vap.) [5]	1320 (*s*, *o*)	886 (*s*, *q*)	—
DNO_3 Raman (liq.) [4]	1300 (*s*)	915 (*s*)	670 (*m*)
DNO_3 Infra-red (vap.) [5]	1313 (*s*, *q*)	888 (*s*, *q*)	—
O_2NO' model [1]			
No. and C_{2v} class Description	4. (B_2) NO_2-stretching	5. (B_2) ONO′-bending	6. (B_1) Out of plane
HNO_3 Raman (liq.) [3]	1675 (*m*, *d*)	610 (*m*, *d*)	(767) [6]
HNO_3 Infra-red (vap.) [5]	1710 (*s*)	583 (*m*, *q*)	765 (*m*, ***Q***)
DNO_3 Raman (liq.) [4]	1645 (*m*)	580 (*m*)	(767) [6]
DNO_3 Infra-red (vap.) [5]	1685 (*s*)	543 (*m*, *q*)	764 (*m*, ***Q***)
H–R model [2]			
No. and C_s class Description	7. (A') H-stretching	8. (A') H-bending	9. (A'') H-twisting
HNO_3 Raman (liq.) [3]	3400 (band)	—	480 (*w*) [7]
HNO_3 Infra-red (vap.) [5]	3560 (*m*)	1335 (*s*, *q*)	465 (*s*, ***Q***)
DNO_3 Raman (liq.) [4]	2470 (band)	—	370 (*w*) [7]
DNO_3 Infra-red (vap.) [5]	2627 (*m*, *Q*)	1014 (*s*, *q*)	(*ca.* 365) [8]

Notes. [1] In these drawings the uppermost mass-point represents the hydroxyl group moving as a single unit. [2] In these drawings the hollow circle represents the hydrogen atom moving relatively to a rigid NO_3 group. [3] As adopted by Ingold and Millen (*loc. cit.*). [4] Bannerji and Mishra, *Indian J. Phys.*, 1941, **24**, 359; Redlich and Nielsen, *J. Amer. Chem. Soc.*, 1943, **65**, 654. [5] This investigation. [6] Not directly observed; deduced from first overtone observed at 1535 cm.$^{-1}$ in the Raman spectrum of both HNO_3 and DNO_3. [7] Recorded by Redlich and Nielsen only (*loc. cit.*). [8] Not observed: estimated from a combination band.

s = strong; *m* = medium intensity; *w* = weak
p = polarised; *d* = depolarised; ***Q*** = strong *Q* branch
Q = medium *Q* branch; *q* = weak *Q* branch; *o* = no *Q* branch

mixing particularly, as we must expect, with the less symmetrical of the other planar-bending frequencies, no. 5.

Under the drawings in Fig. 2 are entered the known Raman fundamental frequencies, as measured in liquid nitric acid and liquid deuteronitric acid. The frequencies assigned to vibrations nos. 1—7 are as given by Ingold and Millen (*loc. cit.*), in agreement with most previous authors. Special comment is necessary on the Raman frequencies of three vibrations.

The frequency of the out-of-plane vibration, no. 6, of nitric acid was for some time doubtful, as Ingold and Millen have recounted; but they should have pointed out in that connexion that, after Freymann and Freymann had observed (*loc. cit.*) an infra-red band in nitric acid vapour at about 780 cm.$^{-1}$, and had suggested that this might be the fundamental band of vibration no. 6, Redlich (*J. Amer. Chem. Soc.*, 1947, **69**, 2240), correcting Redlich and Nielsen's earlier assignment of the Raman frequency 1535 cm.$^{-1}$ to this vibration (*loc. cit.*), recognised the latter frequency at its first overtone, a conclusion supported also by Ingold and Millen. The same conclusion applies to the same Raman frequency of deuteronitric acid.

The frequency of the hydrogen-bending vibration, no. 8, has remained controversial up to the present. Redlich and Nielsen assumed that the line at 1675 cm.$^{-1}$ in the Raman spectrum of nitric acid was double, and that its second component belonged to this vibration. However, their spectrogram showed no signs of the assumed doubling. For the same vibration of deuteronitric acid, they offered a frequency of about 1340 cm.$^{-1}$, represented by a bulge on the microphotometric contour of the strong Raman line at 1300 cm.$^{-1}$. Ingold and Millen could find no signs of a doubling of the Raman frequency 1675 cm.$^{-1}$ of nitric acid. And as to the bulge given by deuteronitric acid, Ingold and Millen found a similar bulge at about 1360 cm.$^{-1}$ on the contour of the strong line at 1300 cm.$^{-1}$, in the Raman spectrum of ordinary nitric acid. It seemed obvious that the two bulges had a common origin, as first overtones of vibration no. 3. The conclusion was, therefore, that the fundamental frequencies of vibration no. 8 had not been observed in Raman spectra. It was noted that they should be weak in Raman, but strong in infra-red spectra; and it was stated that they would be sought by an investigation of the latter. These frequencies have now been located in the infra-red; and, as Ingold and Millen suspected, they are different from the frequencies which had previously been under consideration.

Redlich and Nielsen observed a weak and diffuse line at about 480 cm.$^{-1}$ in the Raman spectrum of liquid nitric acid and one at about 370 cm.$^{-1}$ in that of liquid deuteronitric acid. They assigned these frequencies to the hydrogen-twisting vibration, no. 9. On Ingold and Millen's plates the records of this vibration were too vestigial to justify any firm conclusion. It was noted only that the frequencies should be weak in the Raman spectrum but strong in the infra-red, and it was stated that they would be sought in the latter spectrum. The present study of the infra-red spectrum of nitric acid vapour makes it certain that Redlich and Nielsen's observation and interpretation of these frequencies in the Raman spectra were correct.

The geometry of the nitric acid molecule is relevant to the study of the rotational contours of the vibrational bands in the infra-red spectrum, because any such contour is determined by the magnitudes of the three principal moments of inertia, and by their directions, relatively to that along which the electric moment oscillates in consequence of the vibration.

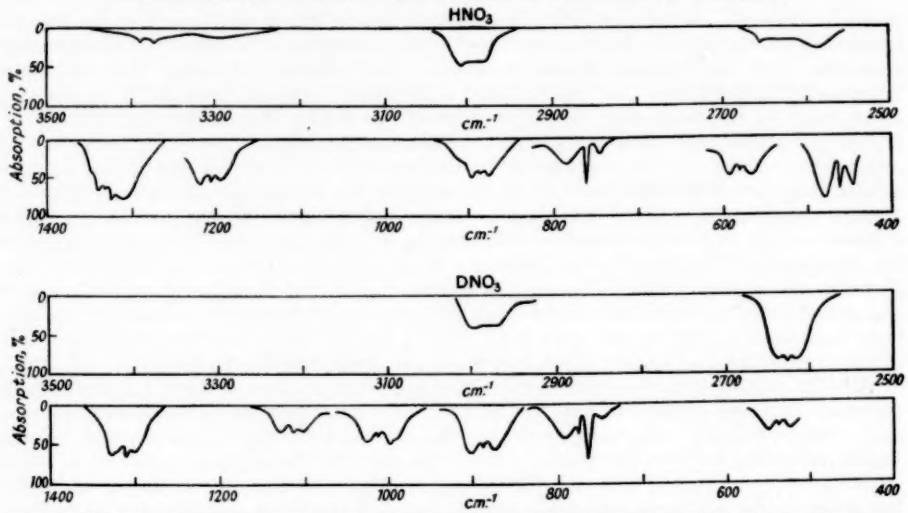
Nitric acid is an asymmetric top; but its mass distribution is not very different from that of the nitrate ion, which is a symmetric top, with two principal moments of inertia each equal to half the third. In nitric acid, the two smaller principal moments of inertia are nearly equal, and the third principal moment of inertia is equal to their sum.

The band envelopes for different types of asymmetric top have been described (Badger and Zumwalt, *J. Chem. Phys.*, 1936, **6**, 711). For molecules of the type of nitric acid, which approximates to a plane symmetric top, the envelopes can take the following forms. (1) For a vibration in which the oscillating electric moment makes a small angle with the axis of the smallest of the principal moments of inertia, the bands will have a Q branch of the same order of intensity as the P and R branches. (2) For a vibration whose electric moment makes a small angle with the axis of the intermediate moment of inertia, the bands will have P and R branches with a central minimum, or at most a small Q branch. (3) For a vibration whose electric moment makes a small angle with the axis of the greatest principal moment of inertia, the bands will have P and R branches separated by an outstandingly strong and sharp Q branch.

In nitric acid the axis of the greatest moment of inertia is certainly at right angles to the molecular plane. However, as to the two axes in the molecular plane, there could be

dubiety as to whether that of the smallest moment of inertia approaches more closely to the C_{2v} axis, or to a direction at right-angles to the latter. In this matter the angle within the NO_2 group could be critical. If the angle is 130°, then, for both nitric acid and deuteronitric acid, according to the model in Fig. 1, the axis of the smallest moment of inertia makes an angle of about 35° with the C_{2v} axis, while the other moment of inertia with an axis in the molecular plane is about 10% larger. If the angle is 135°, then for both acids, the axis of the intermediate moment of inertia makes an angle of roughly 35° in the opposite sense, with the C_{2v} axis, and the other moment of inertia with an axis in the molecular

FIG. 3. *Infra-red absorption bands of nitric and deuteronitric acid vapours*



(The conditions of measurement of each band are as given in Tables 2 and 3. It is to be noted that the conditions are not the same for all the bands, so that relative intensities must be judged with reference to the Tables.)

plane is about 10% smaller. The calculated magnitudes and directions of the principal moments of inertia of nitric acid, and of deuteronitric acid, for the two assumed NO_2 angles, are given in Table 1.

TABLE 1. *Principal moments of inertia* (I_2 *in g.-cm.*^{2}) *of the molecules of nitric and deuteronitric acids, two different* NO_2 *valency angles* (θ) *being assumed.* (I_y *lies in the molecular plane at right-angles to* I_x. I_z *is directed perpendicularly to the molecular plane.*)

θ	Isotope	Angle ($\widehat{I_zC_{2v}}$)	$10^{40}I_x$	$10^{40}I_y$	$10^{40}I_z$
130°	HNO_3	35°	65·0	71·3	136·3
	DNO_3	38°	64·7	74·4	139·1
135°	HNO_3	−30°	70·4	64·8	135·2
	DNO_3	−40°	73·5	64·1	137·6

Now although the forms of band envelopes furnish one of the criteria which help us to assign infra-red bands to their vibrations, we have other means of doing this in the case of nitric and deuteronitric acids, *e.g.*, by comparisons with the Raman spectra of these acids, already fairly completely understood, and by comparisons with the understood Raman and infra-red spectra of the nitrate ion. Thus the infra-red spectra of nitric and deuteronitric acids themselves allow us to form an opinion as to whether the axis of the smallest, or that of the intermediate moment of inertia forms the smaller angle with the C_{2v} axis. The spectra show that it is the axis of the intermediate moment of inertia which does so, and that therefore, the other geometrical parameters of Fig. 1 being accepted, the angle 135° is the better value of the valency angle within the NO_2 group.

Freymann and Freymann (*loc. cit.*) examined the infra-red spectrum from 1600 to 600 cm.$^{-1}$ of nitric acid vapour enclosed between rock-salt plates. These were rapidly attacked by the acid with the production of a nitrate ion spectrum. However, the following observed bands were attributed to nitric acid :

683, 780, 905, (?) 1258, (?) 1572 cm.$^{-1}$

We confirm the second and third of these bands, but not the first, even though there is a Raman frequency of nitric acid having just this value, while the fourth and fifth were not observed by us, unless they correspond to bands which we found at considerably higher frequencies.

Our infra-red frequencies of nitric and of deuteronitric acid, as measured in vapour enclosed between silver chloride plates, and also the particulars of the conditions in which the bands were measured are recorded in Tables 2 and 3, while the forms of the bands, as far as we determined them, are shown in Fig. 3. The last column of either Table contains our assignment of the frequencies to fundamental vibrations or to combination tones. The assignments are given in terms of the numerical labels in Fig. 2.

TABLE 2. *Infra-red absorption bands of nitric acid vapour.*

Frequency (cm.$^{-1}$)	Cell-length (cm.)	Temp. of liquid acid	Slit-width (mm.)	Prism	Assignment
3560	8	20°	0·03	SiO_2	(7)
3390	15	,,	0·06	CaF_2	2 × (4)
3000	,,	,,	0·07	,,	(1) + (4)
{2627	,,	,,	0·08	,,	2 × (1)
{2585	,,	,,	,,	,,	(2) + (4)
1710	4	0	0·20	,,	(4)
{1335	,,	,,	0·32	,,	(8)
{1320	,,	,,	,,	,,	(1)
1206	15	20	0·46	,,	(6) + (9)
886	4	0	0·32	NaCl	(2)
765	13	20	0·34	,,	(6)
583	15	,,	—	KBr	(5)
465	4	0	—	,,	(9)

Note. The braces in the first column denote overlapped bands.

TABLE. 3. *Infra-red absorption bands of deuteronitric acid vapour.*

Frequency (cm.$^{-1}$)	Cell-length (cm.)	Temp. of liquid acid	Slit-width (mm.)	Prism	Assignment
2980	15	20°	0·06	CaF_2	(1) + (4)
2627	8	,,	,,	,,	(7)
1685	4	0	0·16	,,	(4)
1313	,,	,,	0·28	,,	(1)
1114	15	20	0·20	NaCl	(6) + (9)
1014	3	,,	0·24	,,	(8)
888	4	0	0·36	,,	(2)
764	13	20	0·34	,,	(6)
543	15	,,	0·60	KBr	(5)

The assignment of the bands presents no major difficulty. The moderately strong band of nitric acid at 3560 cm.$^{-1}$, as well as that of deuteronitric acid at 2627 cm.$^{-1}$, can at once be assigned to the hydrogen-stretching vibration, no. 7. The contour of the nitric acid band was not determined, but that of the deuteronitric acid band was : it shows P, Q, and R branches of comparable strength, indicating that the oscillating electric moment makes a small angle with the axis of the smallest of the principal moments of inertia. This is in agreement with the already stated conclusion that it is the axis of the intermediate moment of inertia which approximates most closely to the C_{2v} axis, and that, therefore, the wider of the two suggested angles for the NO_2 group of nitric acid is the more nearly acorrect.

The frequencies of the three NO-stretching vibrations, can immediately be recognised, apart from one small detail, by comparison with the Raman spectra, where these frequencies are identified by intensity and polarisation. The strong infra-red band of nitric

acid at 1710 cm.$^{-1}$, and that of deuteronitric acid at 1685 cm.$^{-1}$, obviously belong to vibration no. 4. Their band envelopes were not traced in detail. The strong band of nitric acid at 886 cm.$^{-1}$, as well as that of deuteronitric acid at 888 cm.$^{-1}$, equally clearly belong to vibration no. 2. The envelopes of these bands were traced: they have weak Q branches, indicating that the oscillating electric vector is making only a small angle with the axis of the intermediate moment of inertia. In this vibration the oscillating electric moment lies nearly parallel to the C_{2v} axis, and thus we have confirmation of the conclusion that it is the axis of the intermediate moment of inertia which approximates the most closely to this axis. One component of the strong double band of nitric acid at 1320—1335 cm.$^{-1}$, as well as the strong single band of deuteronitric acid at 1313 cm.$^{-1}$, must belong to vibration no. 1. The higher-frequency component of the nitric acid band has a vestigial Q branch, while the lower-frequency component is of irregular form, but seems to have a central minimum. In the band of deuteronitric acid the lateral branches are irregular, but there seems to be a central minimum. Any of these bands would, so far as the band envelopes can indicate, qualify for assignment to a vibration, such as no 1, in which the electric vector oscillates in a direction near to that of the C_{2v} axis, and therefore by our former conclusion, to that of the axis of the intermediate moment of inertia. We cannot unequivocally decide, nor is it important to do so, which of the two overlapped nitric acid bands should be chosen for assignment to vibration no. 1. Provisionally we have chosen the lower frequency, 1320 cm.$^{-1}$, which gives slightly better values for the calculated frequencies of some combination tones, and slightly more probable isotopic relations.

The second of the overlapped bands of nitric acid, that at 1335 cm.$^{-1}$ according to the above selection, must correspond to the single deuteronitric acid band at 1014 cm.$^{-1}$ The latter is the only band in the relevant frequency region, not needed for other correlations and assignments, and, indeed, the only one with the right type of contour. Like the nitric acid band at 1335 cm.$^{-1}$, the deuteronitric acid band at 1014 cm.$^{-1}$ has a very weak Q branch. Therefore our previous conclusions indicate that these frequencies belong to a vibration in which the electric moment oscillates in a direction approximating to that of the C_{2v} axis. The large isotope shift points to a hydrogen vibration. It follows that these frequencies belong to vibration no. 8. The general order of magnitude of the frequencies, the fact that they are weak to invisibility in the Raman spectrum, and the obviousness with which all other infra-red frequencies except these can be otherwise assigned, all support the conclusion stated.

The frequencies of the bending vibrations, nos. 3 and 5, of the NO_3 group are found in the Raman spectra, where they are clearly distinguished by polarisation. In the relevant region of either infra-red spectrum, only one band appears, in that of nitric acid at 583 cm.$^{-1}$, and in that of deuteronitric acid at 543 cm.$^{-1}$. These bands must belong to vibration no. 5. It is not inconsistent that, in our records of these bands, the Q branches appear to be weaker than the P and R branches, instead of being of the same order of intensity, as is expected for a vibration, such as no. 5, in which the oscillating electric moment is nearly perpendicular to the C_{2v} axis, and therefore nearly parallel to the axis of the smallest moment of inertia. For here, in the potassium bromide range of the spectrum, the low energy in the incident radiation necessitates the use of a slit so wide open that it cannot scan the Q-branch without including parts of the lateral gaps, and therefore records the Q branch with too small an intensity. Vibration no. 3 seems to be too weak in the infra-red to be observed with our equipment: presumably the change of electric moment is quite small in this vibration. It should be mentioned that Freymann and Freymann record an infra-red band of nitric acid in just the right position, namely, at 683 cm.$^{-1}$; but with three times their path-length, we could not find it. We could find a band at 650 cm.$^{-1}$, but the variability of its intensity showed that it did not belong to nitric acid, and we assign it as the strong bending frequency of nitrogen dioxide, a small amount of which often appears in the vapour of nitric acid. Freymann and Freymann were working in the presence additionally of the nitrate-ion band at 720 cm.$^{-1}$, and hence the actual appearance of their spectrum, in the region of the claimed nitric acid band, must have been rather complicated.

The frequencies of the out-of-plane vibration, no 6, of the NO_3 group are clearly identified by the outstandingly strong and sharp Q branches of the nitric acid band at 765 cm.$^{-1}$

and the deuteronitric acid band at 764 cm.$^{-1}$: the vibrating electric moment is now nearly parallel to the axis of the greatest moment of inertia. These frequencies occur too weakly for observation in Raman spectra, but can be deduced from observed Raman overtones.

The frequency of the hydrogen twisting vibration, no. 9, in which also the oscillating electric moment is nearly parallel to the axis of the greatest moment of inertia, is clearly identified for nitric acid by the sharp, prominent, Q branch of the band at 465 cm.$^{-1}$. It must be remembered that the real peak intensity of the Q branch of this band of the potassium bromide region must be much greater than the intensity with which, owing to the large slit-width used, the Q branch appears in our record. The corresponding band of deuteronitric acid lay outside the spectral range of our equipment, consistently with its assignment to a hydrogen vibration, having a large isotopic shift. From an infra-red combination tone, the frequency can be roughly (say to $\pm$10 cm.$^{-1}$) estimated as 365 cm.$^{-1}$. The frequencies of this vibration have already been identified by Redlich and Nielsen in Raman spectra, but owing to the extreme weakness with which they there appear, the present confirmation is useful.

Several combination bands have been measured. Our assignments of them are in Tables 2 and 3.

The frequency differences between vapour and liquid (see Fig. 2) deserve remark : all can be qualitatively understood as arising from intermolecular hydrogen bonding in the liquid. The stretching frequencies of the NO_2 group (vibrations nos. 1 and 4) are reduced on passing from the vapour to the liquid, obviously because, outside each oxygen atom, the hydrogen atom of another molecule is furnishing a restoring force opposite to that of the covalent bond. The stretching frequency of the N–(OH) bond (vibration no. 2) is, however, raised in the liquid, presumably because the oxygen atom is to some extent anchored by the rather closely fixed position, which its laterally bonded hydrogen atom assumes on account of hydrogen-bonding; and perhaps because the oxygen atom itself is anchored by hydrogen-bonding on the side opposite to the covalently bound hydrogen atom. The bending frequency of the O–N–(OH) angle (no. 5) is raised in the liquid—a result which we would expect also for the bending frequency of the O–N–O angle (no. 3), if the observations could be made—because all the oxygen atoms will be directly or indirectly anchored against lateral motion by hydrogen-bonding. The out-of-plane vibration of the NO_2 group shows no change of frequency from vapour to liquid, presumably because nearly all the motion is in the nitrogen atom, which, moving through the plane of the other atoms, is free from hydrogen-bonding. The hydrogen-stretching vibration (no. 7) has its frequency reduced and spread in the liquid, because hydrogen bending opposes various restoring forces to that of the covalent bond. The hydrogen-twisting frequency (no. 9) is increased and spread in the liquid—and we should expect the same result for the hydrogen-bending frequency (no. 8), if we could make the necessary observations—because of the anchoring effect of hydrogen-bonding on lateral hydrogen motion.

As to the isotopic frequency-shifts (see Fig. 2), the Teller–Redlich rule for the isotopic ratios of frequency products is not very useful in application to nitric acid, because, owing to the low symmetry of that molecule, it handles the frequencies in considerable sets. However, Redlich and Nielsen have shown (*loc. cit.*) that the planar Raman frequencies of nitric acid and deuteronitric acid are consistent with the rule. The same is true for the infra-red frequencies.

More interesting information is afforded by some of the individual isotopic frequency shifts. Such shifts measure the amount of motion suffered by the hydrogen atom in the vibration; but, if the hydrogen motion is sufficient to produce a considerable shift, then, on account of amharmonicity in the potential function, the actual shift may be somewhat different from, and is usually a little less than, that computed for harmonic motion.

If the six vibrations (nos. 1—6) of the NO_2 group were completely uncoupled from the three hydrogen vibrations (nos. 7—9), so that in the former set of vibrations the OH group moved exactly as an atom, then the isotope shifts in these vibrations would be small. By neglecting changes of coupling within the set of NO_2 vibrations, it can be computed that none of the shifts would be above 2·0%, the maximum applying to the hypothetical case in which both the OH and NO_2 groups move like single atoms. In fact, five of the six vibra-

tions of the NO_3 group show frequency shifts in the range 0·0 to 1·5%. But one vibration, no. 5, shows a shift of 7%, or more accurately, an isotopic ratio, H : D, of 1·074. Here there must be considerable coupling with one of the hydrogen vibrations. Now if the hydrogen-bending vibration, no. 8, were fully uncoupled from all other vibrations, and also were strictly harmonic, then its isotopic ratio would be 1·403. The observed ratio is only 1·316. That is, the isotopic shift is 7% too small for a pure hydrogen vibration. Thus, a transfer of shift between vibrations nos. 5 and 8 seems to have occurred, and we may reasonably attribute this to the appreciable coupling between these vibrations, which was expected (p. 4274) on the basis of a general consideration of the mechanics of the nitric acid molecule.

If the hydrogen-stretching vibration, no. 7, were fully uncoupled and harmonic, its isotopic ratio, H : D would be 1·388. The observed ratio is 1·355. The defect of 2% is not markedly greater than the defect expected to arise from Morse-curve anharmonicity. It is possible, however, that some of the observed small defect comes from very weak coupling between this vibration and others.

If the hydrogen-twisting vibration, no. 9, were fully uncoupled and harmonic, its isotopic ratio would be 1·397. The observed ratio is only about 1·27, a defect of about 9%. It is unlikely that more than a small part of this defect is due to coupling with other vibrations. Certainly there is no transfer of isotopic shift to the only other vibration of the same symmetry class, namely, vibration no. 6, which in fact shows no shift. Therefore we attribute the large defect in the frequency shift of vibration no. 9 to an abnormal anharmonicity. This is inconsistent with our picture of the twisting vibration as a restricted rotation, for which the potential-energy hollow has a more open shape than either a parabola or a Morse curve, and is, indeed, usually thought to resemble a cosine curve. In such more open hollows, the energy level of the greater-amplitude quantum of the lighter isotopic form can drop down rather closer to that of the smaller-amplitude quantum of the heavier form, thus giving an abnormally small frequency ratio.

By assuming a rotation-restricting barrier of cosine form with two minima, and then neglecting anharmonicity up to the level of the first quantum of torsional oscillation, one may use the frequency of the latter, in order to make a rough computation of the barrier height. The formula is

$$\omega + 6{\cdot}223\ (V/10^{40}I)^{\frac{1}{2}}$$

where ω is the frequency in wave-numbers, V is the barrier height in cal./mole, and I is the "reduced" moment of inertia, that is, $I_1I_2/(I_1 + I_2)$, where I_1 and I_2 are the moments of the groups of OH and NO_2 for independent rotations about the bond between them. With dimensions as in Fig. 1, except that the angle of the NO_2 group is taken as 135°, I has the value of $1{\cdot}50 \times 10^{-40}$ g.-cm.^{2} The observed torsional frequency for nitric acid, 465 cm.$^{-1}$, then leads to the estimated barrier height, 8·4 kcal./mole. Because of the neglect of anharmonicity in the troughs of the potential-energy curve, this estimate is likely to be too low. Hence it is already obvious that the barrier is much larger than those found in simple organic molecules, such as ethane, methylamine, and methyl alcohol, or even in somewhat more complicated ones, such as *neo*pentane, trimethylamine, and methyl ether, none of which has a barrier higher than 4 kcal./mole.

We can carry the study of the barrier a little further by calculating the entropy of nitric acid from the molecular dimensions and our now complete set of frequencies (convenient formulæ and tables are given by Bright Wilson, *Chem. Reviews*, 1940, **27**, 17), and by comparing the result with the calorimetric value of the entropy (Forsyth and Giauque, *J. Amer. Chem. Soc.*, 1942, **64**, 48). This comparison is in Table 4.

The agreement is as good as the estimated accuracy of the calorimetric value. If we treat the latter as accurate, and also regard all the entropy contributions derived from molecular data as accurate, except that coming from the torsional vibration (no. 9), then we can obtain the entropy contribution of the latter by difference, and from this compute the cosine barrier-height, without using the torsional frequency, and therefore without committing the probably appreciable error of neglecting its anharmonicity. By difference we have for the entropy contribution, 0·67 cal./mole-deg., and from this, with the aid of

TABLE 4. *Standard entropy at 298·1° K of nitric acid vapour* (S^0 *in cal./mole-deg.) as calculated from molecular quantities with neglect of gas-imperfection and anharmonicity, and as obtained calorimetrically.*

Vibrational entropy

No.	1	2	3	4	5	6	7	8	9
$cm.^{-1}$	1320	886	680	1710	583	765	3560	1335	465
S^0	0·03	0·15	0·33	0·00	·047	0·24	0·00	0·03	0·75

Total entropy

Translational	38·25	cal./mole-deg.
Rotational	23·35	,,
Vibrations nos. 1—8	1·25	,,
Vibration no. 9	0·75	,,
Total calculated entropy	63·70	,,
Calorimetric value (Forsyth and Giauque)	63·62 ± 0·10	cal./mole-deg.

Pitzer's thermodynamic tables for cosine barrier oscillators (*J. Chem. Phys.*, 1937, **5**, 469), we find the barrier height 10·2 kcal./mole.

However we compute it,* the energy barrier is clearly too large to be credited to the type of force, probably a repulsive force, which sets up barriers of 1—4 kcal./mole against torsional hydrogen motion in simple saturated organic molecules. Forsyth and Giauque (*loc. cit.*), though they had incomplete spectral data, realised that a considerable torsional barrier existed in the nitric acid molecule, and suggested internal hydrogen-bonding as a possible cause. There must, of course, be electrostatic attraction between the hydrogen atom and both non-hydroxyl oxygen atoms in all orientations of the hydroxyl group: such binding, if strong enough, could overcome the usual sort of repulsive force in the two planar orientations, producing energy minima in these configurations, and energy maxima in the intervening perpendicular orientations. In order to see whether such forces could conceivably produce a barrier of the right size, let us make an approximate calculation of the difference of electrostatic energy between the planar and perpendicular orientations. For this purpose, we take the electric moment of the hydroxyl bond as 1·5D, a value which suits the dipole moments of water and alcohols, and assume for simplicity that electric charges giving this moment are located at the hydrogen and oxygen nuclei, while a charge of half an electron, arising from the split dipolar bond, is situated at each of the other oxygen nuclei. The bond lengths and bond angles being taken as heretofore, the electrostatic barrier height then works out to 14·5 kcal./mole. Of course, this type of calculation is very rough; but it does suffice to show that electrostatic binding could, possibly after overcoming the more usual barrier-giving forces of opposite sign, produce a torsional barrier, such as that to which the observations point, with a height of the order of 10 kcal./mole.

EXPERIMENTAL

Pure nitric acid and dinitrogen pentoxide were made as described in earlier papers from these laboratories, while deuteronitric acid was prepared by carefully regulated interaction of the pentoxide with deuterium oxide of 99·6% isotopic purity.

The spectra were recorded on a Hilger D 209 spectrometer, with the prisms and slit-widths specified in Tables 2 and 3.

The cells had silver chloride windows, each about 20 mm. × 25 mm. and 1 mm. thick. Otherwise they consisted only of glass and "polythene." Each window was sealed, by means of a cement of molten "polythene," on to the edges of a hole cut out of the centre of a "polythene" disc of about 5 mm. thickness. The disc was similarly sealed to the rim of the glass cylindrical wall of the cell. This wall carried a branched side-tube: one branch led through a B24 ground joint to a bulb containing the liquid acid, while the other branch led through a tap

* If we had used the dimensions of the crystal molecule of nitric acid (Lazzati, *loc. cit.*) for calculating the rotational entropy of the gaseous molecule when computing the entropy of torsional motion from calorimetric data, the torsional entropy would have been 0·80 cal./mole-deg., and the barrier height 9·2 kcal./mole. Having passed from the frequency direct to the entropy as in Table 4, with neglect of anharmonicity, if we had proceeded from this value to the barrier height with the aid of Pitzer's tables, the value would have been 9·6 kcal./mole.

to the vacuum pump. The acid was held at liquid–air temperature during evacuation of the cell, in preparation for a set of spectral observations.

After making a general survey of a spectrum, the individual bands were examined, by choosing for each a cell of suitable length, and by operating at a suitable vapour pressure, the latter regulated by controlling the temperature of the liquid acid. The object of setting up these conditions, which are specified in Tables 2 and 3, was to produce records showing between 30% and 80% maximum absorption. The practice was to run through the part of the spectrum under investigation, with the conditions thus chosen, and then, without altering the position of the cell, to put a bath of liquid air round the side-bulb, and run through the spectral range again, in order to record the background.

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820. *Infra-red Spectrum of Crystalline Potassium Perchlorate. Reassignment of the lower Fundamental Frequencies of the Perchlorate Ion.*

By (the late) HENRY COHN.

The infra-red spectrum of crystalline potassium perchlorate contains a strong band at 628 cm.$^{-1}$ and a strong double band at 1090, 1140 cm.$^{-1}$. Crystalline nitronium perchlorate shows the same bands. These frequencies are found also in the Raman spectra. However, the other two Raman frequencies, 935 and 460 cm.$^{-1}$, do not appear in the infra-red. It is concluded that the assignments of frequencies to the two stretching vibrations of the perchlorate ion have been correctly made in the past, but that the two bending frequencies have been wrongly assigned, and must be interchanged.

THE perchlorate ion, as a tetrahedral XY_4 molecule, has its nine vibrational degrees of freedom distributed in four normal modes of vibration, as shown in the Table below.

No.	Class	Description
1	A_1	Totally symmetrical, stretching : the four bonds extend synchronously.
2	E	Doubly degenerate, bending : external atoms converge in pairs.
3	F_2	Triply degenerate, stretching : such that external atoms move towards a common direction.
4	F_2	Triply degenerate, bending : the bonds bend over towards a common direction.

All four vibrations are allowed in the Raman spectrum. Observations of the Raman spectra of aqueous solutions of perchlorates have established the existence of three strong Raman frequencies, while the expected fourth is replaced by a diffuse band. Redlich, Holt, and Biegeleisen (*J. Amer. Chem. Soc.*, 1944, **66**, 13) have assigned these frequencies as follows :

(1) A_1 stretching	(2) E bending	(3) F_2 stretching	(4) F_2 bending
935	630	1050—1170	460 cm.$^{-1}$

However, the arguments underlying these assignments are not all equally convincing.

On account of the outstanding intensity of the Raman frequency 935 cm.$^{-1}$, its assignment to vibration no. 1 may be considered well founded. For a time there was doubt about the origin of the band, 1050—1170 cm.$^{-1}$: it was not obvious why vibration no. 3 should produce a broad band. However, Millen accounted for this (*J.*, 1950, 2606), when he found the band replaced by two lines, of frequencies 1080 and 1130 cm.$^{-1}$, in the Raman spectra of crystalline perchlorates. As he noted, this is the simplest result which could arise from near-degeneracy between a degenerate fundamental F_2 at about 1120 cm.$^{-1}$ and the highly degenerate combination $E + F_2$ at $630 + 460 = 1090$ cm.$^{-1}$; for in the symmetric force-field of a crystal, the resulting resonance could yield only two degenerate Raman-active energy levels, while in the instantaneously dissymmetric and fluctuating field of a solution, the degeneracies of these levels would become split, and the split levels broadened, to give six, individually diffuse, Raman-active levels, that is, a band. This is

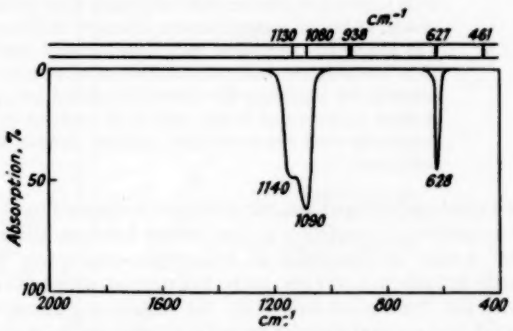
such a consistent interpretation, that the correlation of the band, or of the doublet, with vibration no. 3 seems well confirmed.

It could be considered almost certain, simply on grounds of intensity, that the Raman frequencies 460 and 630 cm.$^{-1}$ belong collectively to the bending vibrations, nos. 2 and 4. This conclusion receives some confirmation from their joint involvement in the above explanation concerning vibration no. 3. However, the reason given by Redlich, Holt, and Biegeleisen for distributing these two frequencies as they did between the two vibrations was not convincing. Herzberg arranged them, though apparently arbitrarily, in the opposite way (" Infra-red and Raman Spectra," van Nostrand, New York, 1945, p. 167). Millen pointed out that the question was open.

Of the four vibrations of the perchlorate ion, only two, namely, the F_2 vibrations, nos. 3 and 4, are allowed in the infra-red spectrum. Therefore this spectrum should furnish a clear distinction between the bending frequencies: vibration no. 4 should record its frequency, while no. 2 should not. If the assignment of frequencies to vibration no. 3 is thought to want further support, then the reappearance of these frequencies in the infra-red would supply the needed confirmation. If any doubt remained as to the assignments of the strongest Raman frequency to vibration no. 1, support for the assignment would follow from the non-appearance of this frequency in the infra-red.

The infra-red spectrum of crystalline potassium perchlorate is shown in the Figure.

Below: *Infra-red spectrum of crystalline potassium perchlorate.*
Above: *Diagram of Raman frequencies for comparison.*



There is a strong single band at 628 cm.$^{-1}$, and also a strong double band with a peak at 1090 cm.$^{-1}$ and a nearly resolved second component at 1140 cm.$^{-1}$. No other band was found over the range 450—2000 cm.$^{-1}$, though a very weak band was observed at about 2050 cm.$^{-1}$. The strong single band, shifted however to 620 cm.$^{-1}$, and the strong double band, have been found again in the infra-red spectrum of crystalline nitronium perchlorate, which will be described in detail later.

These results make it certain that the frequencies of the two bending vibrations of the perchlorate ion have been wrongly assigned in the past, and must be interchanged. The new data confirm previous assignments to the two stretching vibrations. The revised assignments are summarised below (frequencies in cm.$^{-1}$):

	(1) A_1	(2) E	(3) F_2 *	(4) F_2
Raman (soln.)	935	460	1050—1170	630
,, (cryst.)	938	461	1080, 1130	627
Infra-red (cryst.)	— †	— †	1090, 1140	624

* Resonance with (2) + (4). † Forbidden

The weak infra-red band at about 2050 cm.$^{-1}$ can be understood as the allowed combination (1) + (3).

Experimental

A paste of potassium perchlorate in " Nujol " was spread in a thin layer on a plate of sodium chloride or potassium bromide. A comparison plate was prepared in which the scattering effect of the solid perchlorate in the relevant spectral region was approximately imitated by previous grinding of the plate surface.

A Hilger D 209 spectrometer was used, with fluorite, rock salt, and potassium bromide prisms. However, in these experiments the automatic recording arrangements were not employed. Instead, the experimental and comparison plates were mounted side by side, so that either could be inserted in the optical path, and a point-by-point determination of the bands was made by interchanging the plates, and noting the deflections of the secondary galvanometer.

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821. *The Reversibility of the Adsorption of Catalyst Poisons. Part I. The Revival of Poisoned Catalysts by Simple Washing.*

By E. B. MAXTED and G. T. BALL.

The desorption of thiophen, methyl sulphide, and mercury and zinc ions from a platinum catalyst has been examined by treating poisoned catalysts with various changes of a washing liquid, and it has been found possible completely to remove the poison. Similar results were obtained for the desorption of thiophen from a nickel surface, complete removal being, however, reached with somewhat greater difficulty than with platinum. With cadmium ions on nickel, although a considerable recovery in the activity of the poisoned catalyst was observed, complete re-activation was not reached in the present work. This washing method constitutes an alternative to the revival of a poisoned catalyst by changing the state of an adsorbed poison into a shielded form, as studied in previous work, and is of interest both from the standpoint of its simplicity and since metallic poisons cannot be dealt with by chemical detoxication.

IF a dilute solution of a catalyst poison is allowed to remain in contact with a limited amount of a catalyst, a partition of the poison between the adsorbed and the free phase occurs in such a way as to suggest an adsorption–desorption equilibrium even with strong poisons. Little is known, however, as to the rate at which this equilibrium state can be approached from the desorption side with, for instance, poisons such as sulphur compounds or toxic metal ions on platinum or nickel hydrogenation catalysts: indeed, the adsorption of these and other types of strong poisons is sometimes considered to constitute cases of catalyst poisoning which are in practice substantially irreversible, at any rate at room temperature.

As an approach to measurements of the order of the length of the mean adsorbed lives of typical poisons, it was considered of interest to examine the ease with which these can be removed from platinum or nickel surfaces by repeated dilution of the liquid phase, namely, by simple washing of the poisoned surface with a suitable solvent. This is of some practical importance since, if desorption can be obtained easily and rapidly, it should be possible in this way to revive a poisoned catalyst; and this simple washing method should form a useful alternative to the revivification of a poisoned catalyst by chemical detoxication, *i.e.*, by changing the state of the adsorbed poison from a so-called non-shielded to a shielded state (Maxted *et al.*, *J.*, 1940, 252; 1945, 204, 763, 766; 1946, 23; 1947, 624; 1948, 1091, 1093, 1916; *J. Soc. Chem. Ind.*, 1948, **67**, 93; *Chem. and Ind.*, 1951, 242). The desorption method, moreover, is applicable for the removal of metallic poisons, which cannot be detoxicated by chemical treatment.

EXPERIMENTAL

The platinum catalyst used was made from chloroplatinic acid by alkaline formate reduction, the final stages in the washing being carried out by vigorously shaking the stock of catalyst with repeated changes of water until the activity had become constant. For the work with nickel, a stock of Raney nickel was prepared by Covert and Adkins's method (*J. Amer. Chem. Soc.*, 1932, **54**, 4116), modified by the use of water saturated with hydrogen for the washing in order to minimise any oxidation.

The hydrogenation tests, by means of which the restoration of the activity of poisoned

catalysts as a result of the revivification treatment was studied, were carried out in a hydrogenation shaker operated under standardised conditions in a thermostat at 30°. *cyclo*Hexene, in acetic acid solution, was used as a standard unsaturated substance in the hydrogenation runs with platinum. This was also employed, in alcoholic solution, in the tests on the degree of revivification of nickel poisoned with thiophen. In the corresponding tests of the poisoning of nickel with cadmium ions, crotonic acid in aqueous alcohol was taken.

Revivification of Platinum Poisoned by Sulphur Compounds.—(i) *Desorption of thiophen.* The revival of platinum poisoned with thiophen is shown in Fig. 1, in which the hydrogen absorbed is plotted against the time. Curve I relates to a blank run, with an unpoisoned catalyst, the system hydrogenated consisting of 0·025 g. of stock platinum black and 1 c.c. of *cyclo*hexene, dissolved in 9 c.c. of acetic acid. Curve II shows the corresponding hydrogenation of a similar system containing 10^{-5} g.-mol. of thiophen. For the hydrogenation test shown in Curve III, 0·025 g. of platinum was first poisoned with the same amount of thiophen as in Curve II, in 10 c.c. of acetic acid, and shaken for 15 minutes in a closed pipette (in the absence of

FIG. 1. *Removal of thiophen from platinum.*

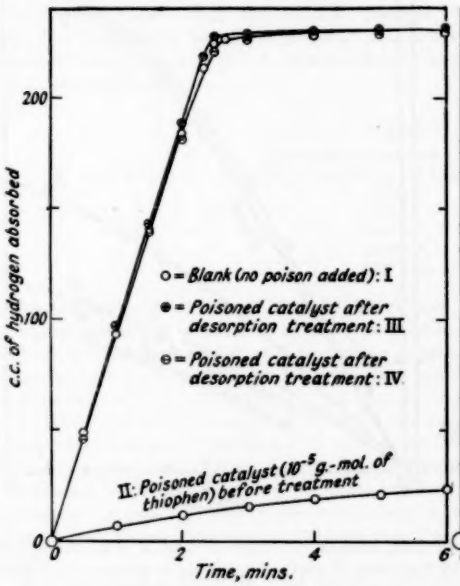
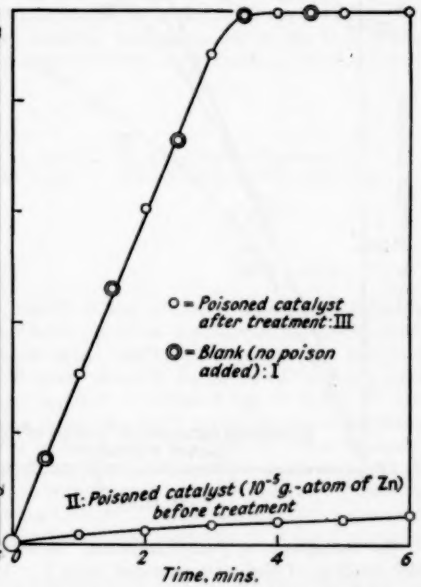


FIG. 2. *Removal of zinc ions from platinum.*

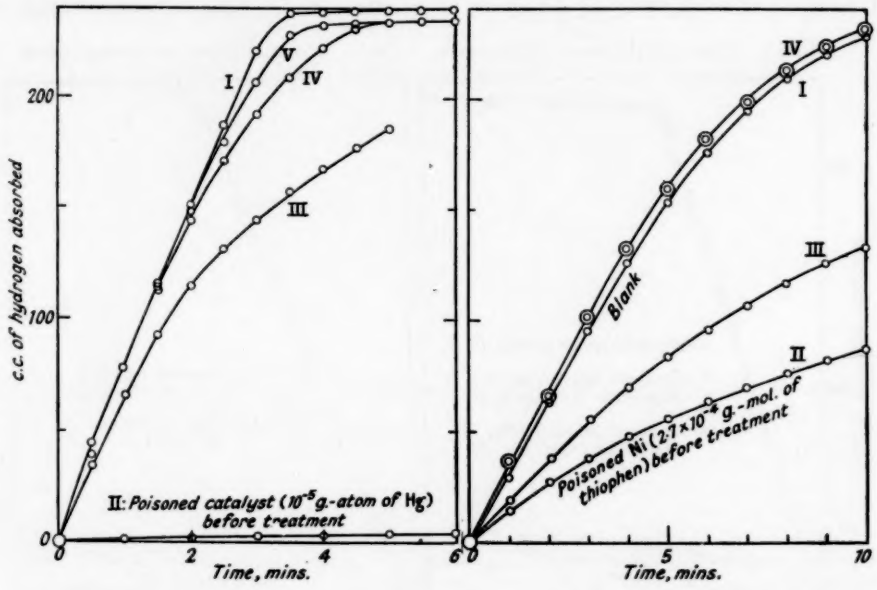


hydrogen) to allow the adsorption of the poison. The solvent was then removed from the poisoned catalyst by centrifuging and decanting, after which the catalyst was washed at room temperature by shaking for 15 minutes with a fresh charge of 10 c.c. of acetic acid in order to try to remove poison from the adsorbed state into the free liquid phase. The supernatant liquid was again removed by centrifuging and decantation as before, and, finally, a charge of 10 c.c. of acetic acid containing 1 c.c. of *cyclo*hexene was added (when presumably more of the poison would move from the adsorbed into the liquid phase) and the activity of the platinum was tested by hydrogenation. The liquid over the poisoned catalyst had thus been changed twice, namely first from the original poisoning solution to a fresh charge of acetic acid and, secondly, from this to the hydrogenation charge. Curve IV shows a similar run, in which only one change of liquid (from the poisoning solution to the hydrogenation charge) was applied. It will be seen from the figure that both of these runs are substantially identical with the blank run; indeed, the thiophen has been almost completely desorbed from the catalyst by one wash. However, the degree of dilution after each centrifuging, namely, the dilution of the small amount of residual liquid still adhering to the 0·025 g. of platinum black to the normal volume of 10 c.c., is of course rather great even for a single change of liquid. This relatively easy removal of thiophen by a single wash should be compared with the desorption of mercury ions (Fig. 3) which are only partly

desorbed by one change of liquid and seem to be bound more strongly to platinum than thiophen and to have a longer adsorbed life.

A further point was also examined with regard to thiophen. Since, in the above treatment, the system had been shaken either once or twice in the absence of hydrogen, it was necessary to make sure that the disappearance of poisoning was not due to the rather unlikely oxidation of the poison on platinum by traces of air during the shaking. To this end, a poisoned charge as in Curve II was shaken in air for two periods of 15 minutes, with centrifuging between and after the two treatments with air but without at any time changing the liquid, *i.e.*, without extraction of the poison, after which the activity of the catalyst was tested by hydrogenation. The hydrogenation curve was still substantially identical with Curve II, indicating that no poison had been removed by oxidation.

FIG. 3. *Removal of mercury ions from platinum.* FIG. 4. *Removal of thiophen from nickel.*



(ii) *Desorption of methyl sulphide.* A set of runs, similar to those of Fig. 1, was carried out with 0·025 g. of platinum poisoned with 4×10^{-6} g.-mol. of methyl sulphide in place of thiophen. Complete re-activation of the catalyst was obtained by changing the liquid above the poisoned platinum twice, with shaking and centrifuging as already described; indeed, as for thiophen, a nearly complete desorption of the poison was reached even after only one change. In the case of methyl sulphide, a little detoxication by oxidation in the presence of the platinum could be detected after shaking the poisoned system with air, but without any change of liquid up to and including the final hydrogenation. In this respect, methyl sulphide differs from thiophen, which cannot be oxidised directly by air at room temperature.

Revivification of Platinum Poisoned by Toxic Metals.—(i) *Desorption of zinc ions.* The hydrogenation system used in this series of tests contained 0·025 g. of stock platinum catalyst, as before, together with a 10-c.c. charge of liquid containing 1 c.c. of *cyclo*hexene, 8·5 c.c. of acetic acid, and 10^{-5} g.-mol. of zinc acetate dissolved in 0·5 c.c. of water. This amount of poison was sufficient to reduce the activity of the platinum to a low value (Curve II of Fig. 2) relative to that given in the blank run (Curve I), in which the poison was omitted. In the hydrogenation test shown in Curve III, the poisoned catalyst, after having been used for Curve II, was separated by centrifuging and washed for 15 minutes at room temperature with 10 c.c. of water, which was then removed by centrifuging, following which a fresh hydrogenation charge of 8·5 c.c. of acetic acid, 0·5 c.c. of water, and 1 c.c. of *cyclo*hexene was added for the hydrogenation test. It will be seen that the original activity of the previously poisoned catalyst has been completely

restored, although this catalyst had already been used for Curve II; indeed, in a further test with another specimen of a similarly poisoned catalyst, an almost complete extraction of the poison was reached even with one change of supernatant liquid. With this poison there is, of course, no question of detoxication by oxidation.

(ii) *Desorption of mercury ions.* The system used was identical with that employed for zinc, save that the catalyst was poisoned with 10^{-5} g.-atom of mercury, applied as the acetate. Curves I and II of Fig. 3 refer, as before, respectively to a blank run and to a poisoned run before any washing treatment. It will be seen from the very low hydrogenation rate of Curve II that mercury ions are more toxic to platinum than the same amount of zinc (cf. Curve II of Fig. 2). The progressive revival of the catalyst by desorption of the mercury ions, as a result of one, two, and three replacements of the supernatant liquid as previously described, is shown respectively in Curves III, IV, and V of Fig. 3, water being used as the washing liquid. The slower desorption rate of this poison, *i.e.*, the longer adsorbed life on the platinum compared with that of thiophen or zinc, was indicated by a lesser degree of response to a single change in the solvent over the poisoned catalyst. The slowness of the removal of the last traces of the poison was further confirmed by two parallel runs, in the second of which the time of shaking with two changes of solvent was increased from the normal period of 15 minutes to 30 minutes for each wash. The slight but consistent benefit in employing a longer washing time is shown in the two hydrogenation runs given in Table 1, which refers in each case to 0·025 g. of platinum poisoned with 10^{-5} g.-atom of mercury.

TABLE 1.

	Hydrogen adsorption (c.c.) with 0·025 g. of poisoned platinum	
Time (mins.)	After 2 washes of 15 mins. each	After 2 washes of 30 mins. each
1	77·0	78·4
2	144·2	148·8
3	191·7	205·3
4	221·3	231·4
5	232·7 (satd.)	232·3 (satd.)

Revivification of Poisoned Nickel.—Work with nickel is less accurate than with platinum, since charges of the catalyst cannot be weighed out as required on account of the oxidisability of the finely-divided metal in a dry state. Approximately uniform amounts were, however, measured out from a paste of Raney nickel stored under alcohol, by means of a small glass bucket attached to a glass dipping rod and having a capacity of about 0·5 g. of nickel for each test. The individual charges of nickel, after being poisoned, were protected from oxidation during the subsequent treatment for the desorption of the poison by using a closed extraction and centrifuging vessel provided with a tap through which the vessel could be evacuated and the air replaced by hydrogen, the unsaturated substance being added only immediately before the hydrogenation run. It was shown, by testing, that the activity of the nickel was not appreciably affected by this shaking and centrifuging unless the liquid was changed to remove adsorbed poison.

(i) *Desorption of thiophen from nickel.* The hydrogenation charge in this series consisted of 0·5 g. of nickel, poisoned by $2·7 \times 10^{-4}$ g.-mol. of thiophen in 11 c.c. of alcohol, 1 c.c. of *cyclo*hexene as before being used as the unsaturated substance. Curves I and II of Fig. 4 show, respectively, a blank hydrogenation run in which the poison had been omitted and a poisoned run in the presence of the above amount of thiophen. In any subsequent treatment of poisoned catalysts, 12 c.c. of water, which had previously been saturated with hydrogen to avoid oxidation of the nickel, were used as the washing liquid. Curve III was given by a catalyst which, after having been poisoned with $2·7 \times 10^{-4}$ g.-mol. of thiophen, had been subjected to two washes of one hour each, with centrifuging as before between each change of liquid. Since the poison was obviously being desorbed from the nickel with greater difficulty than from platinum (cf. Fig. 1), a fresh charge of nickel was first poisoned with thiophen as in Run II of Fig. 4 and then given a more extended washing treatment consisting of four successive washes of 1, 14, 1, and 1 hour respectively. It will be seen from Curve IV that this treatment completely removed the poison. Actually, the activity of the washed catalyst was a little above that in the blank run, but this was probably due to the above-mentioned slight uncertainty in measuring out precisely the same amount of nickel for each hydrogenation run.

(ii) *Desorption of cadmium ions from nickel.* It had been found in previous work that cadmium ions were poisonous towards nickel, sulphate ions being non-toxic, and this metal was accordingly applied as the sulphate. The 12-c.c. hydrogenation charge used in this series con-

sisted of 7 c.c. of water containing 5×10^{-4} g.-mol. of cadmium sulphate, 5 c.c. of alcohol containing 0·01 mole (0·86 g.) of purified crotonic acid, and 0·5 g. of the Raney nickel. Water, previously freed from dissolved air, was used as the washing liquid for the subsequent desorption of the adsorbed cadmium ions from the catalyst. In order to examine the response of the poisoned catalyst to the washing treatment, the usual succession of hydrogenation tests was carried out, namely, first a blank run in the absence of the poison, secondly, a poisoned run in the presence of the above amount of cadmium and, finally, a series of tests with catalysts which, after having been poisoned, had been subjected to various degrees of washing with successive 12-c.c. charges of water. The results of these hydrogenation tests are summarised in Table 2, in which the volume of hydrogen absorbed during an initial 5 minutes period in each test is given as an approximate indication of the activity.

TABLE 2.

State of catalyst	C.c. of hydrogen absorbed (5 min.)
Unpoisoned catalyst (blank run)	116
Catalyst poisoned with 5×10^{-4} g.-atom of Cd^{2+}	32
Poisoned catalyst after 2 washes of 1 hr. each	64
Poisoned catalyst after 3 washes of 2 hrs. each	72
Poisoned catalyst after 4 washes of 1, 14, 1, and 1 hr. each, respectively	76

It will be seen that, although a progressive improvement in the activity of the poisoned catalyst was obtained as the number and length of the washes was increased, a complete restoration to the original activity was not reached for cadmium on nickel. This may, however, have been due to some slight oxidation of the Raney nickel during the prolonged washing treatment.

THE UNIVERSITY, BRISTOL. [*Received, June 14th*, 1952.]

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822. *Aryl-2-halogenoalkylamines. Part X.* The Preparation of Some Derivatives of 1-Aryl-3 : 4-dihalogenopyrrolidines and 1 : 4-Bis-arylamino-2 : 3-dihalogenobutanes.*

By J. J. ROBERTS and W. C. J. ROSS.

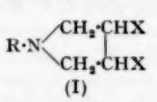
The preparation of 1-aryl-3 : 4-dihalogenopyrrolidines (I; X = halogen) and 1 : 4-di(arylamino)-2 : 3-dihalogenobutanes (II; X = halogen) and some related compounds has been examined. Although it has not proved possible to obtain the halogen compounds without substituents in the aromatic ring two 3 : 4-dibromopyrrolidines, probably the 1-(2 : 4 : 6-tribromophenyl) and 1-(3 : 5-dibromo-2 : 4 : 6-trimethylphenyl) derivatives and also 2 : 3-dibromo-1 : 4-di-(2 : 4 : 6-trimethylanilino)butane have been prepared. The *cis*- and the *trans*-isomers of (I; R = Ph, X = $O{\cdot}SO_2{\cdot}C_6H_4Me$) and the DL- and the *meso*-isomer of (II; R = Ph, R′ = Me, X = $O{\cdot}SO_2{\cdot}C_6H_4Me$) have been obtained. The rates of hydrolysis in aqueous acetone of these derivatives have been determined.

IT has been shown (Ross, *J.*, 1949, 183; Kon and Roberts, *J.*, 1950, 978) that a large number of di-2-halogenoalkylarylamines possess a powerful cytotoxic activity and inhibit the growth of transplanted animal tumours; also that such compounds are mutagenic (Bird, *Nature*, 1950, **165**, 491) and carcinogenic (Haddow, unpublished). In all the compounds tested so far the two reactive halogen atoms were attached to flexible alkyl chains, and in their reactions with biological material attachments could occur at sites very close together (for example, with a single amino-group; Davis and Ross, *J.*, 1949, 2831) or in the case of the compounds prepared by Kon and Roberts (*loc. cit.*) at sites separated by as much as 18 Å. In connection with the hypothesis that the dihalogenoalkylamines produce their characteristic biological effects by means of a cross-linking alkylation reaction (Goldacre, Loveless, and Ross, *Nature*, 1949, **163**, 667) it was of interest

* Part IX, *J.* 1951, 2706.

to prepare compounds in which the alkylating centres were situated at a known and fixed distance apart.

This paper describes attempts to prepare two such types of compound : the pyrrolidine derivatives (I; X = halogen) and 1 : 4-bisarylamino-2 : 3-dihalogenobutanes (II; X = halogen). Two routes to each of these derivatives were examined; in the first the corresponding diol (I or II; X = OH) was the intermediate and in the second the pyrroline (III) or the butene (IV).



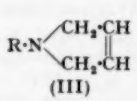
(I)

RR'N·CH$_2$·CHX·CHX·CH$_2$·NRR'

(II)

RR'N·CH$_2$·CH:CH·CH$_2$·NRR'

(IV)



(III)

Compounds (I) via *Dihydroxypyrrolidines.*—Przybytek (*Ber.*, 1884, **17**, 1091) studied the reaction between aniline and *meso*-1 : 4-dichlorobutane-2 : 3-diol and claimed to have obtained 1 : 4-dianilinobutane-2 : 3-diol (II; R = Ph, R' = H, X = OH). A low yield of this diol has now been obtained when DL-1 : 4-dibromobutane-2 : 3-diol is heated in benzene with aniline but heating *meso*- or DL-1 : 4-dichloro- or DL-1 : 4-dibromobutane-2 : 3-diol with three or four equivalents of aniline without solvent gives *cis*- or *trans*-3 : 4-dihydroxy-1-phenylpyrrolidine (I; R = Ph, X = OH). Since it has been claimed (G.P. 805,522; *Chem. Abs.*, 1952, **46**, 1049) that vacuum-distillation of 1 : 4-dianilinobutane-2 : 3-diol (m. p. 111—112°; apparently prepared from aniline and butadiene diepoxide) gives 3 : 4-dihydroxy-1-phenylpyrrolidine, butanediols may be intermediates in the reaction in absence of solvent, being converted into pyrrolidine derivatives at the higher temperature attained. The *cis*- and *trans*-dihydroxypyrrolidines are also obtained when methylaniline is heated with either of the dichlorohydrins, probably by decomposition of a quaternary pyrrolidine salt formed as intermediate.

Attempts to convert these diols into the dichloro-derivatives by phosphorus oxychloride alone or with phosphorus pentachloride failed (contrast Ross, *loc. cit.*), and no dibromo-compound could be isolated after heating of the diols with ethyl bromoacetate and triphenyl phosphite (cf. Landauer and Rydon, *Chem. and Ind.*, 1951, 313) or after treatment of the diacetates with saturated aqueous hydrobromic acid for four days (contrast Wilson and Lucas, *J. Amer. Chem. Soc.*, 1936, **58**, 2396). It was, however, possible to prepare the di-*p*-toluenesulphonates. Reaction with sodium iodide in acetone (the *cis*-compound reacts at approximately twice the rate of the *trans*-derivative at 110°) gave only an unidentified product in poor yield.

Since *NN*-di-2-toluene-*p*-sulphonyloxyethylaniline inhibits tumour growth, having properties very similar to those of *NN*-dihalogenoethylanilines (Timmis, 27th Annual Report of the British Empire Cancer Campaign, p. 43) the toluene-*p*-sulphonates (I; X = O·SO$_2$·C$_6$H$_4$Me) were deemed adequate for testing of the cytotoxic potentialities of structure (I).

Compounds (I) via *Pyrrolines.*—Reduction of 3 : 6-dihydro-2-phenyl-1 : 2-oxazine (Arbuzov, *Doklady Akad. Nauk. S.S.S.R.*, 1948, **60**, 993) yields a product which when distilled in steam (Arbuzov, *ibid.*, 1948, **63**, 531) or dehydrated with phosphoric acid (Wichterle and Vogel, *Coll. Czech. Chem. Comm.*, 1949, **14**, 209), affords phenylpyrroline (III; R = Ph). The preparation of 1-phenyl-Δ^3-pyrroline by reaction of 1 : 4-dibromobut-2-ene with aniline appears to have been considered by von Braun and Lemke (*Ber.*, 1922, **55**, 3536) but they did not obtain sufficient of the base for characterisation or analysis. It is now found that the phenyl-Δ^3-pyrroline may be conveniently prepared by condensing *cis*-1 : 4-dibromobut-2-ene with aniline in hot benzene.

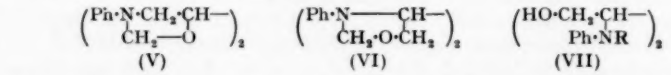
Bromination of (III; R = Ph) with two equivalents of bromine in chloroform solution or when dissolved in aqueous hydrobromic acid gave a monobromo-derivative, which is 1-*p*-bromophenyl-Δ^3-pyrroline since it is also obtained by the reaction of *cis*-1 : 4-dibromobut-2-ene with *p*-bromoaniline. With a large excess of bromine this product yielded a pentabromide provisionally formulated as 3 : 4-dibromo-1-(2 : 4 : 6-tribromophenyl)- and pyrrolidine. In an attempt to avoid bromination of the aromatic ring, 1-*p*-methoxyphenyl-(2 : 4 : 6-trimethylphenyl)-Δ^3-pyrroline were prepared and brominated, but the only

identifiable product was a tetrabromo-compound from the mesidine derivative—probably 3 : 4-dibromo-1-(3 : 5-dibromo-2 : 4 : 6-trimethylphenyl)pyrrolidine. The formation of 3 : 5-dibromo-compounds from mesidine derivatives has been reported by Adams and Dankert (*J. Amer. Chem. Soc.*, 1940, **62**, 2191).

Compounds (II) via *Butanediols.*—From aniline and *meso*-1 : 2-3 : 4-diepoxybutane Przybytek (*loc. cit.*) obtained 1 : 4-dianilinobutane-2 : 3-diol (II; R = Ph, R′ = H, X = OH); he confirmed its identity by analysis of the dihydrochloride, but gave no melting points. It is now found that aniline and DL-1 : 2-3 : 4-diepoxybutane give *dl*-1 : 4-dianilinobutane-2 : 3-diol, m. p. 109° (dipicrate, m. p. 185°). Methylaniline similarly gives DL-1 : 4-di-*N*-(methylanilino)butane-2 : 3-diol, m. p. 102·5° (II; R = Ph, R′ = Me, X = OH) (dipicrate, m. p. 191°; diacetate, m. p. 133°) which is also readily obtained by methylating the diol, m. p. 109°, with methyl iodide. The diol, m. p. 109°, reacts with formaldehyde to yield a dioxazolidine derivative (V), m. p. 184—186°.

When aniline reacts with the 1 : 2-3 : 4-diepoxybutane obtained by epoxidation of 3 : 4-epoxybut-1-ene with perbenzoic acid (Everett and Kon, *J.*, 1950, 3131), the resultant DL-diol, m. p. 109°, already described, is accompanied by an approximately equal amount of an isomer, m. p. 163° (dipicrate, m. p. 180°; forming a dioxazolidine, m. p. 176·5°) which is almost certainly *meso*-1 : 4-dianilinobutane-2 : 3-diol formed from the *meso*-diepoxide in the mixture. Methylaniline similarly gives the diol, m. p. 102·5°, described above and the *meso*-isomer, m. p. 77° (dipicrate, m. p. 184°; diacetate, m. p. 115°).

The view that neither of the diols is a 1 : 4-diol formed by the opening of the epoxide rings in 1 : 2-3 : 4-diepoxybutane at the non-terminal carbon atoms is supported by the similar rates of hydrolysis of their ditoluene-*p*-sulphonates (see below) and by formation of a third isomeric diol, m. p. 116° [dioxazolidine derivative (VI), m. p. 152°] by the reaction of DL-2 : 3-dibromobutane-1 : 4-diol with aniline.



(V) (VI) (VII)

In contrast with the ease with which the 2 : 3-diols are methylated it has not been possible to methylate the 1 : 4-diol (VII; R = H), and methylaniline does not react with the 2 : 3-dibromide. Formation of (VII; R = Me) would be expected to be difficult for steric reasons. The difference supports the view that the diols formed from diepoxybutane and an aromatic base are 2 : 3-diols.

As in the case of the dihydroxypyrrolidines, the butane-2 : 3-diols could not be converted into halogen derivatives, and the ditoluene-*p*-sulphonates were submitted to biological testing.

Compounds (II) via *Butenes.*—Substituted 1 : 4-diaminobut-2-enes have been prepared by the reaction of 1 : 4-dibromobut-2-ene with alkyl- or aryl-amines. For example, Willstätter and Wirth (*Ber.*, 1913, **46**, 535) obtained *NNN′N′*-tetramethyl-1 : 4-diaminobut-2-ene from dimethylamine and von Braun and Lemke (*loc. cit.*) prepared 1 : 4-dianilinobut-2-ene from aniline. *NNN′N*-Tetraethyl-1 : 4-diaminobut-2-ene (IV; R = R′ = Et) and 1 : 4-dipiperidino- and 1 : 4-dimorpholino-but-2-ene have now been synthesised for the study of the bromination of the ethylenic double bond: 1 : 4-Dianilino- (IV; R = Ph, R′ = H), 1 : 4-bis-*N*-methylanilino- (IV; R = Ph, R′ = Me), 1 : 4-bis-*N*-ethylanilino- (IV; R = Ph, R′ = Et), 1 : 4-di-*p*-anisidino- (IV; R = *p*-MeO·C_6H_4, R′ = H), and 1 : 4-di-(2 : 4 : 6-trimethylanilino)-but-2-ene have also been prepared as potential intermediates by allowing the appropriate arylamine to react with *trans*-1 : 4-dichloro- or *trans*-1 : 4-dibromo-but-2-ene.

Bromination of 1 : 4-dipiperidinobut-2-ene afforded the 2 : 3-dibromo-compound, isolated as the dihydrobromide, but 1 : 4-dimorpholinobut-2-ene yielded only the dihydrobromide of the original butene. Only polymeric products were obtained by the action of bromine on *NNN′N′*-tetraethyl-1 : 4-diaminobut-2-ene.

The greater susceptibility of the aromatic ring to attack by bromine, compared with the ethylenic bond—already noted for the arylpyrrolines (above)—was further manifest in formation of 1 : 4-di-*p*-bromoanilino- and 1 : 4-di-(*p*-bromo-*N*-methylanilino)-but-2-ene

(also obtained from *p*-bromo-*N*-methylaniline and *trans*-1 : 4-dichlorobutene) when the corresponding amines were brominated. The only compound of the required structure obtained was 2 : 3-dibromo-1 : 4-di-(2 : 4 : 6-trimethylanilino)butane (II; R = 2 : 4 : 6-$C_6H_2Me_3$, R′ = H, X = Br); this is being tested biologically.

In view of the correlation between the chemical reactivity of the " aromatic nitrogen mustards " and their biological activity (Ross, " Advances in Cancer Research," Vol. I, Academic Press, 1952), the hydrolysis rates of some of the new compounds are recorded in the annexed Table.

No.	Compound †		% Hydrolysed in 50% acetone at 66°
1	$[NPhMe\cdot CH_2\cdot CH(OTs)\cdot]_2$	*meso*	60% in 30 min.
2	"	DL	62% in 30 min.
3	(I; R = Ph, X = OTs)	*cis*	<1% in 120 min.
4	"	*trans*	"
5	(I; R = 2 : 4 : 6-$C_6H_2Br_3$, X = Br)		<1% in 180 min.
6	(I; R = 2 : 4 : 6 : 3 : 5-$C_6Me_3Br_2$, X = Me)		<1% in 240 min.
7	$Ph\cdot N(CH_2\cdot CH_2\cdot OTs)_2$ *		100% in 30 min.
8	$[Ph\cdot N(CH_2\cdot CH_2\cdot OTs)\cdot CH_2\cdot]_2$		"
9	$Me\cdot SO_2\cdot O\cdot[CH_2]_n\cdot O\cdot SO_2\cdot Me$	$n = 2$ *	<1% in 120 min.
10	"	$n = 3$ *	3·5% in 120 min.
11	"	$n = 4$ *	13% in 120 min.
12	"	$n = 6$ *	11% in 120 min.
13	$(TsO\cdot CHMe\cdot)_2$		<1% in 120 min.
14	$CH_2(CHMe\cdot OTs)_2$		5% in 30 min.
15	$([CH_2]_5>N\cdot CH_2\cdot CHBr\cdot)_2$		40% in 30 min.
16	$(2 : 4 : 6\text{-}C_6H_2Me_3\cdot NH\cdot CH_2\cdot CHBr\cdot)_2$		52% in 30 min.; 100% in 360 min.

* Kindly made available by Mr. G. M. Timmis of this Institute. † OTs = $\cdot O\cdot SO_2\cdot C_6H_4Me\text{-}p$.

Foster and Hammett (*J. Amer. Chem. Soc.*, 1946, **68**, 1736) found that the rate of hydrolysis of the ditoluene-*p*-sulphonate of ethylene glycol in aqueous dioxan was about one-twentieth of that of ethyl toluene-*p*-sulphonate. They indicated that the low reactivity could be ascribed to the mutual interaction of the two sulphonyloxy-groups. The relative hydrolysis rates for the toluene-*p*-sulphonates (13 and 14) and the series of methanesulphonates (9—12, Table 1) shows that this deactivating effect decreases as the distance between the sulphonyloxy-groups increases.

The substitution of methylanilino-groups for hydrogen in the terminal methyl groups of compound (13) to give compounds (1) and (2) clearly accelerates hydrolysis. That there is still some retardation due to the proximity of the sulphonyloxy-groups is evident from the rapid hydrolysis of compounds (7) and (8) in which the ester groups are β to the nitrogen atom : these compounds are derivatives of primary alcohols and would be expected to hydrolyse somewhat more slowly than derivatives of unhindered secondary alcohols (compare the relative reactivities of 2-chloroethyl- and 2-chloropropyl-arylamines, Everett and Ross, *J.*, 1949, 1972).

The similar rates of hydrolysis of the two butane derivatives (1) and (2) supports their formulation as *meso*- and DL-isomers of 2 : 3-diols : a sulphonic ester of the 1 : 4-diol (VII) would be derived from a primary unhindered alcohol and would certainly be expected to hydrolyse as fast as compounds (7) and (8).

The nitrogen atom in the β-position to the sulphonyloxy-groups or the bromine atoms in the pyrrolidines (3, 4, 5, and 6) has not the same effect on the hydrolysis rates as is observed in the butane derivatives. This can only be partly due to the fact that there is a single nitrogen atom available for activating both ester groups—compare the hydrolysis rate of *N*-2-chloroethyl-*N*-ethylaniline which is approximately three times that of *NN*-di-2-chloroethylaniline (Ross, *loc. cit.*). The main reason for the lowered reactivity compared with (1) and (2) is probably the restriction imposed by the cyclic pyrrolidine structure on the approach of the activating nitrogen atom to the ester oxygen atom of the toluene-*p*-sulphonyloxy-group or to the bromine atom. Models show that such approach is relatively easy in the butane derivatives.

The hydrolysis rate of the dibromobutane (16) is also slower than would have been expected for an isolated secondary 2-bromoethylamine, thus showing again the retarding influence of the adjacent halogen atom. The fact that the two bromine atoms are

eliminated under these mild conditions supports the formulation of the compound as 2 : 3-dibromo-1 : 4-di-(2 : 4 : 6-trimethylanilino)butane rather than as a compound containing the bromine atoms in the aromatic ring.

Preliminary biological examination indicates that none of the vicinal diesters now described is effective as a tumour-growth inhibitor; in some cases this could have been due to the relatively low chemical reactivity but the biological inactivity in other cases suggests that such close proximity of the alkylating centres does not favour cytotoxic activity.

Experimental

cis-3 : 4-*Dihydroxy*-1-*phenylpyrrolidine*.—(*a*) *meso*-1 : 4-Dichlorobutane-2 : 3-diol (4·5 g.; Owen, *J.*, 1949, 243) and aniline (9 ml.) were heated at 100° for 4 hours. The product was ground with water, and the solid collected by filtration. The *diol* (3·5 g.) remaining after further washing with water and finally with a little ether crystallised from benzene–light petroleum (b. p. 60—80°) as fine needles, m. p. 158·5° (Found: C, 67·3; H, 7·6. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3%).

(*b*) *meso*-1 : 4-Dichlorobutane-2 : 3-diol (1·6 g.) and methylaniline (4·7 g.) were heated at 100° for 5 hours and finally at 130° for one hour. The product, isolated as above, had m. p. 158·5°, undepressed by admixture with *cis*-3 : 4-dihydroxy-1-phenylpyrrolidine prepared by method (*a*).

The diol with acetic anhydride afforded the *diacetate*, m. p. 110·5°, flattened needles from aqueous acetone (Found: C, 63·9; H, 6·5. $C_{14}H_{17}O_4N$ requires C, 63·9; H, 6·5%).

cis-3 : 4-*Ditoluene*-p-*sulphonyloxy*-1-*phenylpyrrolidine*.—Toluene-*p*-sulphonyl chloride (2·6 g.) was added during 15 minutes to an ice-cooled solution of the diol (1 g.) in dry pyridine (4 ml.). The clear solution was then allowed to warm to room temperature. Next day the mixture was diluted with water and the *ditoluene*-p-*sulphonate* (2·8 g.) was filtered off. It formed fine needles, m. p. 162—164°, from aqueous acetone (Found: C, 59·4; H, 5·5. $C_{24}H_{25}O_6NS_2$ requires C, 59·1; H, 5·2%).

trans-3 : 4-*Dihydroxy*-1-*phenylpyrrolidine*.—(*a*) Aniline (4 ml.) and DL-1 : 4-dichlorobutane-2 : 3-diol (1·6 g., Owen, *loc. cit.*) were heated at 100° for 4 hours and then at 140° for 2 hours. The cooled mixture was diluted with water and extracted with benzene. The washed and dried (Na_2SO_4) extract was passsed down a column of activated alumina and the column was eluted with fresh benzene and finally with methanol which removed trans-3 : 4-*dihydroxy*-1-*phenylpyrrolidine* (1 g.), m. p. 123·5—124·5°, prisms from benzene–light petroleum (b. p. 40—60°) (Found: C, 66·7; H, 7·3. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3%).

(*b*) The same diol was obtained when methylaniline (4 ml.) was heated with DL-1 : 4-dichlorobutane-2 : 3-diol (1·6 g.) under the same condition.

The *diacetate* formed plates, m. p. 88·5°, from aqueous methanol (Found: C, 64·1; H, 6·6. $C_{14}H_{17}O_4N$ requires C, 63·9; H, 6·5%). The *di*-p-*toluenesulphonate*, m. p. 153—154°, separated from aqueous acetone (Found: C, 59·1; H, 5·5. $C_{24}H_{25}O_6NS_2$ requires C, 59·1; H, 5·2%).

Reaction of the Above Ditoluene-p-sulphonates with Sodium Iodide.—The ditoluene-*p*-sulphonate (0·5 g.) was heated at 110° with sodium iodide (1 g.) in acetone (8 ml.). The extent of reaction was determined by weighing the precipitated sodium toluene-*p*-sulphonate. After 10 hours' heating the *cis*-compound yielded 320 mg. of the salt and after 15 hours 380 mg. (theor. 380 mg.). In 10 hours only 180 mg. had separated in the case of the *trans*-compound.

1-*Phenyl*-Δ^3-*pyrroline*.—*cis*-1 : 4-Dibromobut-2-ene (21·5 g.) and aniline (27 g.) in benzene (80 ml.) were heated under reflux for 1 hour. The cooled solution was washed several times with water, dried (Na_2SO_4), and evaporated. 1-Phenyl-Δ^3-pyrroline (6 g.) formed prisms, m. p. 100—101°, from methanol (Found: C, 82·4; H, 8·0. Calc. for $C_{10}H_{11}N$: C, 82·7; H, 7·6%). Arbuzov (*Doklady Akad. Nauk. S.S.S.R.*, 1948, **63**, 531) gives m. p. 101—102°.

Bromination. (*a*) Bromine (1·1 g.) in carbon tetrachloride (10 ml.) was added during 30 minutes to a stirred solution of the pyrroline (1 g.) in carbon tetrachloride (40 ml.). The *bromo*-compound which separated crystallised from aqueous methanol as plates, m. p. 126—126·5° (Found: C, 53·2; H, 4·7; N, 5·9; Br, 34·6. $C_{10}H_{10}NBr$ requires C, 53·6; H, 4·5; N, 6·3; Br, 35·6%).

cis-1 : 4-Dibromobut-2-ene (2·1 g.), *p*-bromoaniline (1·7 g.), sodium carbonate (1·5 g.), and benzene (5 ml.) were heated under reflux for 2 hours, then diluted with benzene, washed with water, dried, and evaporated, yielding a residue which crystallised from light petroleum (b. p. 60—80°) as plates, m. p. 126° undepressed by admixture with the monobromide.

(*b*) Bromine (0·64 g.) was added to the pyrroline (0·58 g.) in 48% hydrobromic acid (10 ml.).

Next day the solution was neutralised with ammonia and extracted with ether. The ethereal solution contained the monobromide, m. p. 126°.

(*c*) Bromine (1·95 g.) in chloroform (25 ml.) was added during 10 minutes to a vigorously stirred solution of the phenylpyrroline (0·58 g.) in chloroform (10 ml.). Two days later the chloroform solution was washed with 2N-ammonia, then with water, and dried (Na_2SO_4). The *pentabromide*, obtained on evaporation, formed fine needles (from pentane), m. p. 79° (Found: N, 3·0; Br, 72·4. $C_{10}H_8NBr_5$ requires N, 2·6; Br, 72·9%). The same compound was obtained similarly from the monobromo-derivative.

1-p-*Methoxyphenyl*-Δ^3-*pyrroline*.—*cis*-1 : 4-Dibromobut-2-ene (4·3 g.), *p*-anisidine (2·5 g.), sodium carbonate (2·2 g.), sodium iodide (0·1 g.), and benzene (20 ml.) were heated on a steam-bath for 4 hours. The solution was washed with water and extracted three times with 2N-hydrochloric acid. The combined extracts were decolorised with charcoal, neutralised with ammonia, and re-extracted with ether. Evaporation of the dried (K_2CO_3) ethereal solution yielded the *pyrroline* which crystallised from benzene–pentane as plates, m. p. 118° (Found: C, 75·6; H, 7·2. $C_{11}H_{13}ON$ requires C, 75·4; H, 7·5%).

1-*Mesityl*-Δ^3-*pyrroline*.—*cis*-1 : 4-Dibromobut-2-ene (6·7 g.), mesidine (4·2 g.), anhydrous sodium carbonate (4 g.), and sodium iodide (0·1 g.) in benzene (30 ml.) were heated under reflux for 4 hours. The solution was washed several times with water, dried (Na_2SO_4), and distilled. The fraction of b. p. 90—100°/2 mm. (1·5 g.) was the required pyrroline, characterised as *hydrobromide*, needles (from benzene), m. p. 190—191° (Found: C, 58·4; H, 6·6. $C_{13}H_{17}N,HBr$ requires C, 58·2; H, 6·8%).

Bromination. The pyrroline (1·5 g.) in carbon tetrachloride (20 ml.) was treated with bromine (3 g.) in carbon tetrachloride (40 ml.). After 2 hours at room temperature the solvent and excess of bromine were removed under reduced pressure. The *tetrabromo*-compound formed prisms, m. p. 178—179·5°, from light petroleum (b. p. 60—80°) (Found: C, 31·1; H, 2·0; N, 2·9; Br, 63·9. $C_{13}H_{15}NBr_4$ requires C, 30·9; H, 3·0; N, 2·8; Br, 63·3%).

The pyrroline hydrobromide gave the same product (m. p. and mixed m. p.).

meso- *and* DL-1 : 4-*Dianilinobutane*-2 : 3-*diol*.—1 : 2-3 : 4-Diepoxybutane (2 g.; Everett and Kon, *J.*, 1950, 3131) and aniline (5 ml.) in benzene (10 ml.) were heated under reflux for 4 hours. The solid (3·8 g.) which separated was collected by filtration, washed with a little benzene, and crystallised twice from ethanol. meso-1 : 4-*Dianilinobutane*-2 : 3-*diol* formed prisms, m. p. 163° (Found: C, 71·0; H, 7·5. $C_{16}H_{20}O_2N_2$ requires C, 70·6; H, 7·4%).

The *dipicrate* formed red prisms (from ethanol), m. p. 179—180° (Found: C, 45·8; H, 3·8. $C_{28}H_{26}O_{16}N_8$ requires C, 46·0; H, 3·6%).

The diol (0·5 g.) was shaken for 1 hour with 40% formaldehyde solution (20 ml.). The dried ethereal extract of this mixture yielded meso-3 : 3′-*diphenyldi*(*oxazolidin*-5-*yl*), m. p. 174—176·5°, plates from methanol (Found: C, 72·9; H, 7·1. $C_{18}H_{20}O_2N_2$ requires C, 73·0; H, 6·9%).

Chromatography of the benzene liquors obtained after the separation of the *meso*-diol on activated alumina, and development with benzene and then chloroform, left material on the column which was eluted with methanol and finally crystallised from benzene–light petroleum (b. p. 40—60°). DL-1 : 4-*Dianilinobutane*-2 : 3-*diol* formed plates, m. p. 109—110° (Found: C, 70·4; H, 7·5%). Its *dipicrate*, m. p. 183—185°, formed red prisms from ethanol (Found: C, 45·9; H, 3·8%), and the *di*(*oxazolidine*) derivative formed small prisms (from methanol), m. p. 184—186° (Found: C, 73·4; H, 7·2%).

The same DL-diol, m. p. and mixed m. p. 110°, was obtained when aniline (4·5 g.) and pure DL-1 : 2-3 : 4-diepoxybutane (1·7 g.; b. p. 56—58°/25 mm., m. p. 2—4°; prepared from DL-2 : 3-dibromobutane-1 : 4-diol essentially by the method of Prevost, *Compt. rend.*, 1926, **183**, 1292) in benzene (8 ml.) were heated under reflux for 4 hours.

meso- *and* DL-1 : 4-*Di*-N-*methylanilinobutane*-2 : 3-*diol*.—1 : 2-3 : 4-Diepoxybutane (6 g.; Everett and Kon, *loc. cit.*), methylaniline (18 ml.), and benzene (20 ml.) were heated under reflux for 12 hours. Dilution of the cooled solution with light petroleum (b. p. 40—60°) precipitated DL-1 : 4-*bis*-N-*methylanilinobutane*-2 : 3-*diol* (4·9 g.) which formed fine needles, m. p. 102—102·5°, from benzene–light petroleum (b. p. 40—60°) (Found: C, 72·3; H, 8·4. $C_{18}H_{24}O_2N_2$ requires C, 72·0; H, 8·1%).

The DL-diol was also obtained by similarly condensing pure DL-diepoxybutane with methylaniline. The diol formed a *dipicrate*, m. p. 190—191°, yellow prisms from ethanol (Found: C, 47·8; H, 4·4. $C_{30}H_{30}O_{16}N_8$ requires C, 47·5; H, 4·0%), and a *diacetate* (acetic anhydride in warm pyridine), stout prisms, m. p. 132·5—133·5°, from methanol (Found: C, 68·8; H, 7·6. $C_{22}H_{28}O_4N_2$ requires C, 68·7; H, 7·3%).

The mother-liquors from the original precipitation of the DL-diol were diluted with benzene

(300 ml.) and passed through a column of activated alumina (150 g.). Continued washing with benzene slowly eluted meso-**1** : **4**-*bis*-N-*methylanilinobutane*-**2** : **3**-*diol* (5·8 g.) which formed needles, m. p. 76·5—77° from benzene–light petroleum (b. p. 40—60°) (Found : C, 72·2; H, 8·2%). The *meso*-diol formed a *dipicrate*, m. p. 184°, prisms from acetone (Found : C, 47·8; H, 4·3%), and a *diacetate*, m. p. 114—115·5°, thick prisms from methanol (Found : C, 68·7; H, 7·3%).

Methylation of meso- *and* DL-**1** : **4**-*Dianilinobutane*-**2** : **3**-*diol*.—Methyl iodide (4 g.) in ethanol (10 ml.) was added to the diol (0·5 g.) in boiling ethanol (25 ml.) and heating was continued for 1½ hours. The excess of the methyl iodide and solvent were removed by distillation and an ethereal solution of the residue was washed with dilute aqueous sodium hydroxide, dried, and evaporated. The oily product from the *meso*-diol gave a picrate, m. p. 184°, and from the DL-diol a picrate, m. p. 190°, was obtained. From the recrystallised picrates the same *meso*- and DL-**1** : **4**-di-*N*-methylanilinobutane-**2** : **3**-diols were regenerated which had been obtained directly from methylaniline.

Ditoluene-p-*sulphonates of* meso- *and* DL-**1** : **4**-*Di*-N-*methylanilinobutane*-**2** : **3**-*diols*.—Toluene-*p*-sulphonyl chloride (2 g.) was added during 15 minutes to a stirred, ice-cooled solution of the diol (1·5 g.) in dry pyridine (5 ml.). After being kept at room temperature overnight the mixture was poured on ice and extracted with chloroform. The residue obtained when this extract was washed with 2N-sodium hydroxide, dried, and evaporated solidified on trituration with ether–methanol. The *ditoluene*-p-*sulphonate* of the *meso*-diol formed a micro-crystalline powder [from benzene–light petroleum (b. p. 60—80°], m. p. 142—143° (Found : C, 63·5; H, 6·3. $C_{32}H_{36}O_6N_2S_2$ requires C, 63·2; H, 6·0%), and of the DL-diol formed small prisms, m. p. 145—146° (depressed to 130° by admixture with the derivative from the *meso*-diol) (Found : C, 63·7; H, 6·3%).

DL-**2** : **3**-*Dianilinobutane*-**1** : **4**-*diol*.—DL-**2** : **3**-Dibromobutane-**1** : **4**-diol (2·5 g.) and aniline (5 ml.) were heated at 110° for 4 hours. The mixture was shaken with benzene and water, and the dried benzene layer was evaporated, giving a residue which crystallised from benzene–light petroleum (b. p. 40—60°). DL-**2** : **3**-*Dianilinobutane*-**1** : **4**-*diol* formed plates, m. p. 115—116° (Found : C, 70·6; H, 7·5. $C_{16}H_{20}O_2N_2$ requires C, 70·6; H, 7·4%). When this diol was treated with aqueous formaldehyde as previously described DL-**3** : **3**′-*diphenyldi*(*oxazolidin*-**4**-*yl*), m. p. 151—152°, needles from methanol, was obtained (Found : C, 73·1; H, 7·0. $C_{18}H_{20}O_2N_2$ requires C, 73·0; H, 6·9%).

trans-**1** : **4**-*Dipiperidinobut*-**2**-*ene*.—Piperidine (16 g.) was added during 15 minutes to a cooled solution of *trans*-**1** : **4**-dichlorobut-**2**-ene (5 g.) in benzene (25 ml.). The product was diluted with chloroform and washed with water. Evaporation of the dried chloroform layer gave an oil (5·3 g., 58%) which formed a *dipicrate*, m. p. 191—193°, yellow needles from water (Found : C, 45·8; H, 4·7. $C_{26}H_{32}O_{14}N_8$ requires C, 45·9; H, 4·7%).

By a similar method morpholine afforded trans-**1** : **4**-*dimorpholinobut*-**2**-*ene* (63% yield), m. p. 90—91·5°, prisms from pentane (Found : C, 63·5; H, 10·0. $C_{12}H_{22}O_2N_2$ requires C, 63·7; H, 9·8%).

When diethylamine and the *trans*-dichloride were allowed to react a fraction, b. p. 125°/36 mm., 65—75°/4 mm. (45% yield), forming a dipicrate, m. p. 154°, needles from acetone–ethanol (Found : C, 44·1; H, 5·3. Calc. for $C_{24}H_{32}O_{16}N_8$: C, 43·9; H, 4·9%), was obtained. Amundsen, Mayer, Pitts, and Malentacchi (*J. Amer. Chem. Soc.*, 1951, **73**, 2118) give b. p. 113°/20 mm. for the free base and m. p. 154—155·5° for the dipicrate.

trans-**1** : **4**-*Di*-N-*methylanilinobut*-**2**-*ene*.—*trans*-**1** : 4-Dichlorobut-2-ene (5 g.) and methylaniline (17·5 g.) were heated at 100° for 4 hours. Water was then added and the mixture extracted with ether. Evaporation of the washed and dried (K_2CO_3) extract gave a residue which crystallised from methanol. The trans-*diamine* formed small prisms (6·1 g., 57%), m. p. 77—78·5° (Found : C, 80·7; H, 8·2. $C_{18}H_{22}N_2$ requires C, 81·1; H, 8·3%).

trans-**1** : **4**-*Di*-N-*ethylanilinobut*-**2**-*ene*, m. p. 73—73·5°, prisms from methanol (Found : C, 81·5; H, 9·0. $C_{20}H_{26}N_2$ requires C, 81·6; H, 8·9%), was similarly prepared from ethylaniline (yield, 51%).

A poor yield of *trans*-**1** : 4-dianilinobut-2-ene, b. p. 174—176°/0·4 mm. (Found : C, 80·1; H, 7·7. Calc. for $C_{16}H_{18}N_2$: C, 80·6; H, 7·6%), was obtained from aniline. von Braun and Lemke (*loc. cit.*) record b. p. 235—245°/14 mm. for this base.

trans-**1** : **4**-*Di*-(**2** : **4** : **6**-*trimethylanilino*)*but*-**2**-*ene*.—A mixture of mesidine (6·8 g.), *trans*-**1** : 4-dibromobut-2-ene (5·4 g.), anhydrous sodium carbonate (5 g.), and sodium iodide (0·1 g.) in benzene (50 ml.) was heated for 2 hours on a steam-bath. The benzene solution was then washed with water and extracted with dilute hydrochloric acid. After decolorisation with charcoal the acid extract was neutralised with ammonia and shaken with ether. Evaporation of the dried

(K_2CO_3) ethereal solution gave a residue which crystallised from aqueous methanol or pentane. trans-**1** : **4**-*Di*-(**2** : **4** : **6**-*trimethylanilino*)*but*-**2**-*ene* formed diamond-shaped crystals, m. p. 100·5—102·5° (36%) (Found : C, 82·0; H, 9·3. $C_{22}H_{30}N_2$ requires C, 81·9; H, 9·4%).

A 59% yield of trans-**1** : **4**-*di*-p-*anisidinobut*-**2**-*ene*, m. p. 124·5—125·5°, plates from benzene–pentane (Found : C, 72·7, 72·8; H, 7·7, 7·6. $C_{22}H_{18}O_2N_2$ requires C, 72·5; H, 7·4%), was similarly obtained.

Although *p*-bromoaniline gave no identifiable product when treated with the dibromobutene, *p*-bromo-*N*-methylaniline readily gives a 62% yield of *trans*-**1** : 4-di-(*p*-bromo-*N*-methylanilino)-but-2-ene, m. p. 118°, prisms from light petroleum (b. p. 60—80°), not depressed by admixture with the product obtained by brominating *trans*-**1** : 4-bis-*N*-methylanilinobut-2-ene (see below).

Bromination of trans-**1** : **4**-*Dipiperidinobut*-**2**-*ene*.—Bromine (3·6 g.) in chloroform (20 ml.) was added during ½ hour to a stirred solution of the dipiperidinobutene (2·2 g.) in chloroform (40 ml.). The solvent and excess of bromine were removed under reduced pressure and the semi-solid residue crystallised from methanol. **2** : **3**-*Dibromo*-**1** : **4**-*dipiperidinobutane-dihydrobromide*, m. p. 262° (decomp.), formed small prisms (Found : C, 30·6; H, 4·8. $C_{14}H_{26}N_2Br_2,2HBr$ requires C, 30·9; H, 5·2%).

Bromination of trans-**1** : **4**-*Dianilinobut*-**2**-*ene*.—Bromine (1·6 g.) in chloroform (40 ml.) was added during 1 hour to a solution of the dianilinobutene (2·4 g.) in chloroform (40 ml.) at −20°. The mixture was allowed to come slowly to room temperature and 3 days later the dihydrobromide (2·4 g.), m. p. 208—209° (decomp.), was collected by filtration. trans-**1** : **4**-*Di*-p-*bromoanilinobut*-**2**-*ene* formed prisms, m. p. 134—136°, from benzene–pentane (Found : C, 48·6; H, 4·2. $C_{16}H_{16}N_2Br_2$ requires C, 48·5; H, 4·1%).

Similar bromination of the methylanilinobutene, m. p. 77—78·5°, afforded a hydrobromide, m. p. 172—173° (decomp.), from which trans-**1** : **4**-*di*-(p-*bromo*-N-*methylanilino*)*but*-**2**-*ene*, m. p. 114°, prisms from light petroleum (b. p. 60—80°), was obtained (Found : C, 51·3; H, 4·9. $C_{18}H_{20}N_2Br_2$ requires C, 51·0; H, 4·8%).

2 : **3**-*Dibromo*-**1** : **4**-*di*-(**2** : **4** : **6**-*trimethylanilino*)*butane*.—When the trimethylanilinobutene (1·5 g.; m. p. 102·5°) was brominated as above, a hydrobromide (3 g.), m. p. 210—212°, separated. The free base proved to be the required **2** : **3**-*dibromobutane* derivative, m. p. 152—153° (slow heating), 162° (rapid heating), fine needles from light petroleum (b. p. 40—60°) (Found: C, 54·4; H, 6·5; Br, 33·5. $C_{22}H_{30}N_2Br_2$ requires C, 54·8; H, 6·2; Br, 33·2%).

NN′-*Diphenyl*-NN′-*di*-(**2**-*toluene*-p-*sulphonyloxyethyl*)*ethylenediamine*.—A solution of *NN′*-di-2-hydroxyethyl-*NN′*-diphenylethylenediamine (30 g.) (Kon and Roberts, *J.*, 1950, 978) in dry pyridine (200 ml.) was cooled to 0° and toluene-*p*-sulphonyl chloride (36 g.) was added during ½ hour. The solution was allowed to warm to room temperature and next day was poured into water, and the precipitated *ditoluene*-p-*sulphonate* was filtered off and washed with dilute hydrochloric acid followed by iced water. The ester formed prisms from benzene, m. p. 154—156° (Found : C, 63·4; H, 5·9. $C_{32}H_{36}O_6N_2S_2$ requires C, 63·1; H, 6·0%).

Hydrolysis Rates of the **1** : **2**-*Diesters*.—The hydrolysis rates in 50% aqueous acetone at 66° were determined as described by Ross (*J.*, 1949, 183).

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823. *Aryl-2-halogenoalkylamines. Part XI.* The Reaction of* NN-*Di-2′-chloroethyl-2-naphthylamine with some Phosphoric Acid Derivatives.*

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The reaction of *NN*-di-2′-chloroethyl-2-naphthylamine with some phosphoric acid derivatives has been studied. It has been shown that the competition factors of secondary monoester are much higher than those of primary diester phosphoryl groups. The stability and direction of fission of the diethyl and diphenyl phosphates of di-2′-hydroxyethyl-2-naphthylamine under acid and alkaline conditions have been examined.

Butler, Gilbert, James, and Ross (*Nature*, 1951, **168**, 985) suggested that the degradation of deoxyribonucleic acid preparations which occurs after treatment with "mustards" might be connected with the formation of unstable trisubstituted phosphoric esters by reaction of the primary phosphoryl groups in the nucleic acid with the reagents.

In view of the interest in the reaction of phosphoric acid groups with the cytotoxic agents we report the results obtained when *NN*-di-2′-chloroethyl-2-naphthylamine—a typical "aromatic nitrogen mustard" which has been the subject of clinical trials—reacts with the anions of ethyl, hydroxyethyl, hydroxypropyl, and α- and β-glyceryl dihydrogen phosphate and of diethyl, bishydroxypropyl, and diphenyl hydrogen phosphate.

Experimental.

Materials.—Barium ethyl phosphate. Ethanol (50 ml.) and metaphosphoric acid (20 g.) were heated under reflux for 6 days. The unchanged metaphosphoric acid dissolved when the mixture was poured into water (70 ml.) and the inorganic phosphate formed was precipitated on addition of an excess of barium hydroxide. Carbon dioxide was passed through the heated solution to remove the excess of barium, and the hot solution was filtered. The filtrate was evaporated to 70 ml. and then ethanol (70 ml.) was added. Barium ethyl phosphate separated in an amorphous form which changed into fine needles when left overnight in contact with the mother-liquor. The equivalent weight of the salt was found by titration with acid to phenolphthalein and methyl-orange (Found: equiv., 261. Calc. for $C_2H_5PO_4Ba$: equiv., 261). The method is similar to that of Langheld (*Ber.*, 1911, **44**, 2077) but modifications have been made in the isolation of the barium salt.

Barium tetraethyl diphosphate. Triethyl phosphate (90 g.), hydrated barium hydroxide (80 g.), and water (200 ml.) were heated under reflux for 1½ hours, treated whilst hot with carbon dioxide, and filtered. Barium diethyl phosphate separated on addition of ethanol to the concentrated filtrate. The barium salt was recrystallised by dissolution in the minimum quantity of water and treatment with ethanol (Found: Ba, 30·9. Calc. for $C_8H_{20}O_8P_2Ba$: Ba, 31·0%).

Barium hydroxyethyl phosphate. Tri-2-chloroethyl phosphate (65 ml.), hydrated barium hydroxide (250 g.), and water (700 ml.) were heated under reflux for 16 hours. When the slightly acid solution was rendered alkaline with ammonia a heavy precipitate formed. This was collected by filtering the hot solution and dissolved in cold water (600 ml.); the solution was clarified by addition of Celite and filtration through a Whatman No. 42 paper. Barium monohydroxyethyl phosphate separated when the solution was heated to boiling; it was filtered off from the hot solution and washed with methanol and ether. After several hours' drying at 90° the yield was 22 g. (Found: equiv., 279; Ba, 48·7%. Calc. for $C_4H_{10}O_8P_2Ba$: equiv., 277; Ba, 49·5%).

It was not found possible to prepare barium tetrahydroxyethyl diphosphate by Plimmer and Burch's method (*J.*, 1929, 279). The conditions described by these workers gave only the monohydroxyethyl ester.

Barium 2-hydroxypropyl phosphate. Propylene oxide was added to a hot solution of disodium hydrogen phosphate (250 g.) in water (200 ml.) under an efficient reflux condenser at such a rate that an excess was maintained throughout the 8 hours of the reaction. Water (800 ml.) and an excess of barium hydroxide were added and then the cold solution was filtered. Heating the filtrate caused a heavy precipitate to be formed; this was collected and redissolved in cold water (600 ml.). Heating to 95° caused separation of *barium 2-hydroxypropyl phosphate* which was

* Part X, preceding paper

collected and washed with methanol and acetone. The yield of material dried at 140°/20 mm. for 20 hours was 35 g. (Found: equiv., 291·5; Ba, 46·7%. $C_3H_7O_8PBa$ requires equiv., 291; Ba, 47·1%).

Barium tetra-2-hydroxypropyl diphosphate. An excess of propylene oxide was added, cautiously at first, to orthophosphoric acid (15 ml.; *d* 1·75). After 24 hours most of the unchanged oxide was removed under reduced pressure and hydrated barium hydroxide (37·8 g.) in water (150 ml.) was added to the residue. The solution was allowed to evaporate slowly at room temperature in a vacuum-desiccator. Several weeks later the colourless gum was heated at 160°/0·5 mm. to remove propylene glycol. The residue was dissolved in the smallest quantity of dry ethanol and then poured into sodium-dried ether (800 ml.). The barium salt separated as a microcrystalline solid which was dried at 130°/5 mm. The product was mainly barium tetra-2-hydroxypropyl diphosphate but titration with methyl-orange and phenolphthalein, and also the barium content, showed it to be contaminated with about 6% of monohydroxypropyl ester (Found: Ba, 26·3. $C_{12}H_{28}O_{12}P_2Ba$ requires 24·4%).

The glycerophosphates used were commercial preparations, one being pure β-ester and the other containing 65% of α-ester (periodate titration).

Diphenyl hydrogen phosphate, m. p. 69—70°, from light petroleum (b. p. 60—80°) (Hoeflake, *Rec. Trav. chim.*, 1916, **36**, 24, gives m. p. 70° for the anhydrous acid), was obtained by alkaline hydrolysis of diphenyl chlorophosphonate.

Bis(diethyl phosphate) of NN-di-2′-hydroxyethyl-2-naphthylamine. Diethyl chlorophosphonate (12 g.; McCombie, Saunders, and Stacey, *J.*, 1945, 380) was added during 15 minutes to a solution of *NN*-di-2′-hydroxyethyl-2-naphthylamine (5·8 g.) in 2 : 6-lutidine (12 ml.) at −5°. When the mixture had solidified it was allowed to reach room temperature. Next day water was added and the mixture extracted with ether. The ethereal extract was washed with water, 0·2N-acid, and water again, and finally dried and evaporated. A light brown oil remained, which decomposed on attempted distillation at 10^{-4} mm. Triethyl phosphate (b. p. 210—211°) and 1 : 4-di-2′-naphthylpiperazine (m. p. 230°, undepressed on admixture with a specimen of m. p. 238° prepared by the method of Davis and Ross, *J.*, 1949, 2831) were present in the decomposition products. Analysis of the original oil showed it to be the required *diethyl phosphate* (Found: C, 52·4; H, 7·1; N, 3·1; P, 12·4%; hydrolysis equiv., 254. $C_{22}H_{35}O_8NP_2$ requires C, 52·5; H, 7·0; N, 2·8; P, 12·3%; equiv., 252).

Bis(diphenyl phosphate) of NN-di-2′-hydroxyethyl-2-naphthylamine. To a solution of di-2′-hydroxyethyl-2-naphthylamine (6 g.) in 2 : 6-lutidine (10 ml.) cooled to −10° was added diphenyl chlorophosphonate (11 ml.). During the addition (15 minutes) the temperature rose to 0°. Later as the base hydrochloride began to separate the temperature reached 25°. After a further 4 hours in the ice-bath the mixture was left at room temperature overnight. Water (250 ml.) was added and the ester extracted with ether. The ethereal layer was washed thrice with water (300 ml.) and then with 0·2N-hydrochloric acid until the washings were neutral to Congo-red. The dried ethereal solution was evaporated and the semi-solid residue dissolved in a small quantity of dry benzene, and then 20 volumes of sodium-dried ether were added to the warmed solution. On cooling, flattened needles of the *diphenyl* ester formed, having m. p. 83° (Found: C, 65·6; H, 5·6; N, 2·0; P, 8·9%; hydrolysis equiv., 340. $C_{32}H_{35}O_8NP_2$ requires C, 65·7; H, 5·1; N, 2·0; P, 8·9%; equiv., 348).

Method.—Determination of competition factors. NN-Di-2′-chloroethyl-2-naphthylamine (536 mg., 0·002 mole) was dissolved in neutralised acetone (150 ml.), a solution of the phosphate ester in water (150 ml.) was added, and the mixture rapidly heated to 37° and kept at this temperature for 24 hours. The liberated hydrogen and chloride ions were then titrated with 0·1N-sodium hydroxide and silver nitrate, phenolphthalein and potassium chromate being used as indicators (the use of chromate was more generally applicable than that of dichlorofluorescein in the present work). The competition factors were calculated as described in Part III (*J.*, 1949, 2589). When the barium salts of the phosphoric esters were insoluble in the given volume of water they were converted *in situ* into the sodium salts by the addition of an exact equivalent of sodium sulphate.

The determination of the competition factor of the orthophosphate ion required a special method since in this case the acidity produced under the standard conditions was greater in the presence of the ion than in its absence—the increased rate of reaction being due to the presence of a negatively charged phosphate group on one side chain of the initial reaction product (cf. Davis, Thesis, London, 1950, p. 57)—and it was also impossible to titrate the liberated chloride ion in the presence of the phosphate ion. A normal 24 hour's hydrolysis was carried out and then the acetone was removed under reduced pressure and unchanged chloroethylamine extracted

with ether. The inorganic phosphate in the aqueous layer was determined by precipitation with magnesia mixture and ignition. This gave the amount of unchanged phosphate remaining and a blank run gave the amount originally present : the difference represents the amount of ester formed. The total acidity produced is derived from reactions :

(i) $RCl + H_2O \longrightarrow ROH + H^+ + Cl^-$

(ii) $RCl + Na_2HPO_4 \longrightarrow RNa_2PO_4 + H^+ + Cl^-$

The extent of reaction (ii) is now known and the extent of reaction (i) can be calculated and the competition factor, F, determined as follows :

$$F = \frac{\text{acidity produced by reaction with phosphate ion}}{\text{acidity produced by reaction with water} \times [\text{phosphate}]}$$

The concentration of anion has been expressed in all cases in the terms of normality with respect to dissociating hydrogen. For consistency this has been done even when it is certain that not all the hydrogen ions can have been dissociated at the same time in the reaction mixture (*e.g.*, in the case of the phosphate ion where the pH remained at about 9 throughout the reaction).

Rates of Hydrolysis of Phosphates of Di-2′-hydroxyethyl-2-naphthylamine.—The second-order velocity constants for alkaline and acid hydrolysis of the diethyl and diphenyl phosphates of di-2′-hydroxyethyl-2-naphthylamine in 80% acetone at 50° were determined as described in Parts VIII and IX (*J.*, 1950, 3056; 1951, 2706), with results given in Table 1.

TABLE 1. *Velocity constants for the hydrolysis of esters.*

Ester	10^4k in acid	10^4k in alkali
$2\text{-}C_{10}H_7\cdot N[CH_2\cdot CH_2\cdot O\cdot PO(OEt)_2]_2$	0·33	0·5 *
$2\text{-}C_{10}H_7\cdot N[CH_2\cdot CH_2\cdot O\cdot PO(OPh)_2]_2$	0·55	5·0 *
$2\text{-}C_{10}H_7\cdot N(CH_2\cdot CH_2\cdot OAc)_2$	2·06	4800

* Approximate, probably being too high, since the consumption of alkali by side-reactions with the acetone becomes appreciable with these more slowly hydrolysed esters.

Direction of Fission during the Hydrolysis of the Bis(diethyl phosphate) of Di-2′-hydroxyethyl-2-naphthylamine.—(a) *Acid hydrolysis.* The ester (82·9 mg., 2×10^{-4} mole) was heated under reflux with 0·1N-sulphuric acid (5 ml.) and water (25 ml.) for 40 min. Then 25 ml. were distilled off. The residue required 6·96 ml. of 0·1N-sodium hydroxide on titration; *i.e.*, the total quantity of alcohol liberated was $1·96 \times 10^{-4}$ mole. To the distillate were added 0·3472N-potassium dichromate (5 ml.) and concentrated sulphuric acid (5 ml.), and the solution was heated for 15 minutes on a steam-bath. After addition of water (250 ml.) and potassium iodide (3 g.) the liberated iodine was titrated with 0·1N-sodium thiosulphate. 16·95 ml. were required in the above experiment and 17·35 ml. were required in a blank run. The ethanol liberated thus amounted to $0·10 \times 10^{-4}$ mole, and the ratio, mole of ethanol liberated/mole of hydroxyethylamine liberated, is 0·054. Other determinations gave values of 0·045 and 0·062 for this ratio.

(b) *Alkaline hydrolysis.* The ester (6×10^{-4} mole) was hydrolysed by heating it under reflux with 0·1N-sodium hydroxide (25 ml.) for 3 hours and the extent of the hydrolysis was determined by titration with acid. The ethanol liberated was determined by distillation and oxidation as already described. In this case the ratio, mole of ethanol liberated/mole of hydroxyethylamine liberated, was 0·25, 0·24, 0·18, and 0·21 in four determinations.

These results may be summarised : in the acid hydrolysis of the triester the ethyl ester linkage is attacked at about one-twentieth of the rate, and in the alkaline hydrolysis at one-quarter of the rate, of the aminoethyl ester linkage.

Direction of Fission during the Hydrolysis of the Bis(diphenyl phosphate) of Di-2′-hydroxyethyl-2-naphthylamine.—(a) *Acid hydrolysis.* The ester (200 mg.) was refluxed for 40 minutes with 0·1N-sulphuric acid (10 ml.) in water (40 ml.), and then the mixture was steam-distilled for 20 minutes. The total extent of hydrolysis was determined by titration of the residual solution with alkali, and the liberated phenol was determined in the distillate by bromination (Scott, *Ind. Eng. Chem., Anal. Ed.*, 1931, **3**, 67). In a typical run : ester taken = $2·9 \times 10^{-4}$ mole; total alcohol liberated = $1·7 \times 10^{-4}$ mole; phenol liberated = $0·067 \times 10^{-4}$ mole. It is not possible to define exactly the amount of triester which is converted into diester in the acid hydrolyses since, in contrast to alkaline hydrolyses, where the amount of diester hydrolysed is negligible, some diester is then always attacked. The amount of monoester formed cannot be determined by a phenolphthalein–methyl-orange titration since di-2′-hydroxyethyl-2-naphthylamine interferes with the end-points but the amount clearly cannot exceed 0·067/1·7 (or about

4%) of the total ester hydrolysed since phenol must be formed in the production of monoester. Colorimetric tests show that no inorganic phosphate is formed in these runs. Thus the amount of triester hydrolysed to diester must be equal to, or greater than, $1{\cdot}7 - 2 \times 0{\cdot}067 = 1{\cdot}566$ moles in the above experiment and the ratio, mole of phenol liberated/mole of hydroxyethylamine liberated in the conversion of triester into diester, cannot exceed $0{\cdot}067/1{\cdot}566 = 0{\cdot}043$ and may be much less. In two other runs this ratio was found to be 0·02 and 0·025.

(b) *Alkaline hydrolysis.* The bis(diphenyl phosphate) of di-2′-hydroxyethyl-2-naphthylamine (100 mg.) was heated under reflux with N-sodium hydroxide (2 ml.), water (6 ml.), and ethanol (8 ml.) for 1 hour. This resulted in the complete hydrolysis of triester to diester, as shown by the titration of the residue after steam-distillation, to methyl-orange and phenolphthalein. In each of three determinations the amount of phenol produced corresponded exactly with the amount of hydrolysis occurring, that is, one mole of triester produced one mole of phenol.

These results may be summarised : during the hydrolysis with alkali the diphenyl phosphate is attacked exclusively at the phenyl ester linkage whereas during acid hydrolysis it is the 2-aminoethyl linkage which preferentially undergoes fission.

Discussion

Table 2 shows that anions of phosphoric monoesters have competition factors (F) comparable with those of carboxylic acids (compare Part III where F for the acetate ion was shown to be 100). The values for the glycerophosphates are somewhat lower than for the other monesters; α- and β-glycerophosphate clearly have similar F values. The competition factors of the anions of phosphodiesters on the other hand are very much lower. In view of the reputed instability of triesters of phosphoric acid it was at first

Table 2. *Competition factors of phosphoric acid derivatives.*

	Competition factor (F): Concentration			pH at end of reaction: * Concentration	
Anion	0·01N	0·02N	0·05N	0·01N	0·02N
Orthophosphate	—	108	—	—	8·7
Pyrophosphate	53	45	—	9·3	7·7
Ethyl phosphate	167	152	112	—	8·8
Hydroxyethyl phosphate	117	100	66	—	8·6
2-Hydroxypropyl phosphate	126	134	—	—	8·8
Glycerophosphate (β)	75	66	45	—	—
,, (65% α)	—	68	—	—	—
Diethyl phosphate	—	5·3	3·9	—	3·3
Di-2-hydroxypropyl phosphate	1·2	3	—	—	—
Diphenyl phosphate	—	—	4·4	—	—

* This was the pH of the solution after 24 hours and before titration.

thought that the low F value of the primary diester phosphoryl group might be due to the ready hydrolysis of the triester first formed under the conditions of the determination. It will be seen from Table 2 that owing to the lack of buffering action of the diesters the pH of the solution falls to a greater extent than for the monoesters. However, it was later shown that the diethyl and diphenyl phosphates of di-2′-hydroxyethyl-2-naphthylamine were not appreciably hydrolysed at pH 3 in 50% acetone during 24 hours. This is also confirmed by the results in Table 1 which indicate that these phosphates are more resistant to hydrolysis than the corresponding acetate.

The low F value of the primary phosphoryl group in these simple diesters was rather surprising in view of the high degree of reaction between " sulphur mustard gas " and the primary phosphoryl groups of thymus nucleic acid reported by Elmore, Gulland, Jordan, and Taylor (*Biochem. J.*, 1948, **42**, 308). An investigation carried out in collaboration with Dr. P. Alexander has shown that the competition factor of the carboxyl group in polymethylacrylic acid towards di-2′-chloroethyl-2-naphthylamine is considerably higher than that in a simple carboxylic acid, values of up to 3000 having been obtained. It has been suggested that this high value might be due to the adsorption of the " mustard " on to the polymer, thus facilitating reaction with the nucleophilic groups thereon as opposed to reaction with water. Some similar explanation may apply to the reaction of di-2-chloroethyl sulphide with the primary phosphoryl groups in thymus nucleic acid.

The stability of the phosphoric triesters (Table 1) relative to the acetate was also rather unexpected. This suggests that more stable linkages would be formed by the reaction of chloroethylamines with primary phosphoryl groups in nucleic acids than with carboxylic groups in proteins, though it is realised that structural effects may vitiate this argument. The structures dealt with in this work are much simpler than those likely to be concerned in biological systems. An attempt to prepare a di-2-hydroxyalkyl phosphate of di-2′-hydroxyethyl-2-naphthylamine (which would be a triester more closely related to the product obtained when di-2′-chloroethyl-2-naphthylamine reacts with a pentose nucleic acid—it has a hydroxy-group β to the phosphate linkage) was unsuccessful.

It has been suggested (Butler *et al.*, *loc. cit.*) that the degradation of nucleic acid structures after treatment with chloroethylamine might be due to hydrolysis of triesters formed by the reaction of the halide with primary phosphoryl groups. Should such triesters undergo fission at one of the sugar–phosphate linkages then the nucleic acid chain will be broken. This suggestion prompted the present study of the direction of fission of triesters derived from the biologically active di-2′-chloroethyl-2-naphthylamine. Under alkaline conditions fission occurs exclusively at the " non-mustard " linkage in the case of the diphenyl phosphate and quite appreciably at this linkage in the case of the ethyl derivative. Acid hydrolysis in each case results in preferential hydrolysis of the aminoethyl ester linkage. It is realised that these results are incomplete but there is some support for the hypothesis of Butler *et al.* since it has been shown that esters derived from the reaction of a " mustard " with a primary diester phosphoryl group can hydrolyse with fission at the " non-mustard " linkage.

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824. *The Nature of the Co-ordinate Link. Part VI.* A Comparison of Equilibria between* cis- *and* trans-$(MEt_3)_2PtCl_2$, *where* M = P, As, *and* Sb.

By J. CHATT and R. G. WILKINS.

The isomerisations of *cis*-$(AsEt_3)_2PtCl_2$ and *cis*-$(SbEt_3)_2PtCl_2$ in benzene solutions are endothermic reactions; $\Delta H_{As} = 1{\cdot}2$ kcal. mol.$^{-1}$, $\Delta S_{As} = 14{\cdot}2$ cal. mol.$^{-1}$ deg.$^{-1}$; $\Delta H_{Sb} = 2{\cdot}4$, $\Delta S_{Sb} = 9{\cdot}4$ at 25° (in the same units). The equilibrium mixture of *cis*- and *trans*-arsine complexes at 25° contains only 0·57% of *cis*-isomer, but the stibine equilibrium mixture contains 34·4% as compared with 7·5% for the corresponding equilibrium in the phosphine series. The phosphine and stibine complexes differ in their entropies of isomerisation; the phosphine and arsine complexes in their heats of isomerisation. The total bond strengths of the *cis*-isomers are very approximately 10 kcal. higher than those of their *trans*-isomers. If this difference is due to π-bonding between *d*-orbitals of the platinum and the donor (M) atoms then the strength of the π-component of the M–Pt bond must stay almost constant throughout the series M = P to M = Sb. On the other hand, the strength of the σ-component of the bond must fall from M = P to M = Sb to account for the qualitatively observed weakening of the M–Pt bond. Steric effects would have a negligible effect on these equilibria. Possible causes of the great stability of the tertiary phosphine, arsine, and stibine platinous complexes relative to their trialkylamine analogues are discussed.

THIS study was undertaken to see what further evidence it would reveal for or against the suggestion that electron pairs from *d*-orbitals contribute by π-bonding (partial double-bonding) to the strength of the bond between metals with filled *d*-orbitals, and donor atoms with vacant *d*-orbitals in complex compounds such as $(MR_3)_2PtCl_2$ (Chatt, *J.*, 1949, **3340**, and earlier references quoted therein; *Nature*, 1950, **165**, 637, 859; Part I, *J.*, 1950, **2301**; Part II, *J.*, 1951, **652**; *Research*, 1951, **4**, 180; Wilkins, *Nature*, 1951, **167**, 434; Coates, *J.* 1951, 2003; Part III, Chatt and Wilkins, *J.*, 1951, 2532; Part IV, Chatt and Williams,

* Part V, *J.*, 1952, 273.

J., 1951, 3061; Kabesh and Nyholm, *J.*, 1951, 3245; Part V, *loc. cit.*; Chatt, "The General Chemistry of Olefin Complexes with Metallic Salts," in "Cationic Polymerisation and Related Complexes," Ed. P. H. Plesch, Heffer, Cambridge, 1952).

In Part V, we showed that the total bond energy of *cis*-$(PEt_3)_2PtCl_2$ is about 10 kcal. greater than that of its *trans*-isomer. This we consider to be evidence that *d*-orbitals contribute to a greater (although it could be smaller) extent in the binding of phosphorus than in the binding of chlorine to platinum. This contribution is probably by π-bonding between the *d*-orbitals of the phosphorus and platinum atoms. However, the platinum atom is much larger than the phosphorus atom and, other factors being equal, we should expect π-bonding to be greatest when the atom M is approximately the same size, and uses the same type of *d*-orbital, as the platinum atom, because the π-bond will then be most symmetrical. The tetrahedral covalent radii of the relevant atoms are P = 1·10, As = 1·18, Sb = 1·36, and Pt = 1·31 Å, and the *d*-orbitals used are P = 3*d*, As = 4*d*, Sb = 5*d*, and Pt = 5*d*. On this basis, π-bonding between antimony and platinum should be particularly favoured and it should increase in the order P<As<Sb. On the other hand, the attraction of M for the electrons from *d*-orbitals of the platinum atom will increase as M becomes more electronegative, so on this basis π-bonding should decrease in the order P>As>Sb. We have therefore examined, by the method described in Part V, the equilibrium between *cis*- and *trans*-$(AsEt_3)_2PtCl_2$ and -$(SbEt_3)_2PtCl_2$, and compared the data obtained with those previously published for the triethylphosphine complexes. This work, which we describe below, indicates that the *d*-orbital contribution to the M–Pt bond remains approximately constant throughout the series. It does not prove that the *d*-orbital contribution is by π-bonding since it may be by greater *d*-character of the σ-bonds. However, if it is by π-bonding, which we consider probable in the light of the experiments recorded in Part IV, then the effects of increasing size and decreasing electronegativity of M, operating against each other as the series is ascended from M = P to M = Sb, are almost balanced.

Initially, we chose to investigate equilibria in the tri-*n*-propyl series of complexes, $(MPr_3)_2PtCl_2$, because the solubilities of its members in benzene are more suitable than those of other members of the homologous series (see Wilkins, Report on Co-ordination Chemistry Conference, *Nature*, **1951**, **167**, 434). However, it proved unsuitable for our present purpose. The equilibrium between the arsine complexes lay so far to the *trans*-side that its shift with temperature could not be measured sufficiently accurately to determine the heat and entropy of isomerisation. This is also true of the tri-*n*-butyl and presumably of higher homologues. The trimethyl series of complexes could not be used because its members of *cis*-configuration are almost insoluble in benzene. The triethyl series provided the only compromise in the tri-*n*-alkyl series between insufficient solubility of the *cis*-isomers and unfavourable position of equilibrium between the arsine complexes. The equilibrium mixtures of *cis*- and *trans*-$(AsEt_3)_2PtCl_2$ contains only 0·57% of the *cis*-isomer, but measurements of the shift of equlibrium with temperature, sufficiently accurate to determine ΔH, were just possible with our apparatus.

Using the technique described in Part V, we determined the thermodynamic functions listed in Table 1. The triethylarsine complexes were examined between 15° and 70° and the triethylstibine complex over the range 15—35°.

TABLE 1. *Data relating to the isomerisation* cis ⟶ trans-$(MEt_3)_2PtCl_2$ *in benzene at* 25°.

Substance	*cis*-Isomer in equilm., %	$\log K = A - BT^{-1}$ *A*	*B*	*K* †	$-\Delta G$,† 15°-cal.	ΔH, † 15°-cal.	ΔS † ‡
$(PEt_3)_2PtCl_2$ *	7·5	2·901	540	12·3 ± 0·2	1480 ± 12	2470 ± 210	13·3 ± 0·7
$(AsEt_3)_2PtCl_2$...	0·57	3·108	258	175 ± 10	3060 ± 45	1180 ± 200	14·2 ± 0·8
$(SbEt_3)_2PtCl_2$...	34·4	2·049	527	1·91 ± 0·02	383 ± 8	2410 ± 350	9·4 ± 1·0

* Taken from Part V for comparison. ‡ In 15°-cal. mol.$^{-1}$ degree^{-1}.

† P, As, and Sb will be used as suffixes with these and other symbols to indicate that they refer to the triethyl-phosphine, -arsine, and -stibine complexes and their isomerisation reactions.

Equilibrium Positions and ΔG.—The three equilibrium constants fall in an irregular sequence K_P being intermediate between K_{As} and K_{Sb}. The high equilibrium concentration of the *cis*-isomer in the stibine equilibrium is caused by the relatively low entropy change of the isomerisation reaction and not by exceptionally strong π-bonding between the anti-

mony and platinum atoms, which would have been reflected in a relatively large value of ΔH_{Sb}. This observation again illustrates the importance of entropy changes in equilibria involving highly dipolar molecules such as co-ordination compounds, even of very closely similar types. The very low concentration of *cis*-isomer in the arsine series is caused by the exceptionally low heat of isomerisation, the entropy change ΔS_{As} being comparable with that in the phosphine series.

Entropy Change.—ΔS_P and ΔS_{As} are not significantly different but ΔS_{Sb} is lower than the other two. In Part V we attributed the high value of ΔS_P to greater solvation of the highly dipolar *cis*-$(PEt_3)_2PtCl_2$ compared with its non-polar *trans*-isomer. Jensen (*Z. anorg. Chem.*, 1936, **229**, 250) found the dipole moments of *cis*-$(MEt_3)_2PtCl_2$, where M = P, As, and Sb, in benzene solution to be 10·7, 10·5, and 9·2 D., respectively. He also stated that no correction was made for the spontaneous isomerisation of the complexes in the time which elapsed between making up his solutions and measuring their dielectric constants. By the addition of a trace of the bridged complex, $(AsEt_3)_2Pt_2Cl_4$, to the benzene solutions we were able to depress spontaneous isomerisation, so that its slight effect could be accurately estimated (cf. Part III, *loc. cit.*). Using Jensen's method and formula, we find the moments (μ) of the *cis*-complexes to be $\mu_P = 10{\cdot}9$, $\mu_{As} = 10{\cdot}9$, and $\mu_{Sb} = 10{\cdot}5$ D. These moments are so similar that the decrease in solvation, due to the slightly smaller dipole moment of the stibine complex as compared with those of the other two, could scarcely account for the fairly large differences $\Delta S_P - \Delta S_{Sb}$ and $\Delta S_{As} - \Delta S_{Sb}$. It may be that decreasing dipole moment and increasing molecular size in their effect on solvation are mainly responsible for the observed differences in ΔS, but we should have expected ΔS_{As} to lie a little nearer to the mean of ΔS_P and ΔS_{Sb} if these were the only factors involved.

Heat of Isomerisation, ΔH.—The irregularity in the values of ΔH as the series is ascended is very marked; ΔH_{As} has about half the value of ΔH_P and ΔH_{Sb}. In Part V, we split ΔH_P into three important components: (1) the energy change due to the rearrangement of electric charges which takes place on isomerisation; (2) the difference in heat of solvation of the two isomers from an infinitely dilute gas phase into benzene solution at 25°; (3) the change in bond energy which occurs during isomerisation. Assuming that all the positive charge resides at the centres of the atoms M and the negative charge at the centres of the chlorine atoms so that the platinum atom has zero charge, we have calculated from the dipole moments approximations to (1) (Table 2) (see Part V). The maximum value of (2) is equal to $T\Delta S$, so, using $T\Delta S$ as the real value of (2), we obtain approximations to (3) as shown below. The signs of these heat effects are positive when they represent heat absorption in the isomerisation reaction *cis* ⟶ *trans*; ΔH = (1) + (2) + (3). All are in kcal./mole.

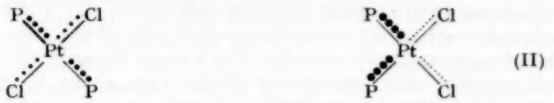
TABLE 2.

Substance	Charge on M and Cl	(1)	(2) = $T\Delta S$	ΔH	(3)
$(PEt_3)_2PtCl_2$	0·341*e*	−13·7	4·0	2·5	12·2
$(AsEt_3)_2PtCl_2$	0·334*e*	−12·7	4·2	1·2	9·7
$(SbEt_3)_2PtCl_2$	0·310*e*	−10·6	2·8	2·4	10·2

The differences in total bond energy (3) between the *cis*- and *trans*-isomers are of course only first approximations. Although (1) may be appreciably in error the true values will fall in regular sequence as do those we give. Thus the observed irregularities in ΔH must be due to irregularities in (3), modified by those in (2). The values of (2) are maximum values, but because ΔS_P and ΔS_{As} are equal, the values of (3) for the phosphine isomers and arsine isomers are comparable. The corresponding value of (3) for the stibine isomers is less certain, because ΔS_{Sb} is much smaller than ΔS_P and ΔS_{As}, and the error in estimating the heat effect associated with ΔS will increase in importance as ΔS increases.

The figures (3) represent approximately the increase in total bond energy when the two MEt_3 groups and Cl atoms are moved from *trans*- to *cis*-positions. We suppose that this increase is due to stronger π-bonding in the M–Pt bond when the M atoms occupy *cis*-positions. Both phosphorus and chlorine have vacant *d*-orbitals so that both the P–Pt and the Cl–Pt bonds could have partial double-bond character. It is assumed that the P–Pt bond has greater double-bond character than has the Cl–Pt bond because phosphorus is higher than chlorine in the *trans*-influence series (see Part IV).

In (I) and (II), we represent by dotted lines, the π, or other bond components in which electron pairs from filled *d*-orbitals of the metal atom contribute in some manner to the strength of the M–Pt and Cl–Pt bonds. The strengths of these components are represented by the size of the dots. In the *trans*-complex (I) both P–Pt bonds must use the same *d*-



orbitals in the π-component : hence the π-components are weaker than in the *cis*-complex where each P–Pt bond has available a different *d*-orbital. On the other hand, the chlorine atoms in the *cis*-complex (II) are now competing with the phosphorus atoms for electrons from *d*-orbitals of the platinum atom, so will get a smaller share than they had in the *trans*-complex. The values (3) thus represent the gain in energy due to the greater double-bond character of the P–Pt bonds when they are in *cis*-relationship, less the loss in energy due to smaller double-bond character of the Pt–Cl bonds. The greater the tendency of electron pairs from *d*-orbitals of the platinum atom to contribute to the P–Pt bond, the greater would be this difference. The values (3) are thus an arbitrary measure of the strength of the π, or other component of the M–Pt bond to which the *d*-orbitals make special contribution. They indicate that the strength of this component stays almost constant as the series is ascended from M = P to M = Sb. This is the only certain information about the M–Pt bond provided by this study.

However, it appears from the values of (3) in Table 2 that the *d*-orbitals contribute more in binding platinum to phosphorus than to arsenic or to antimony. Thus we expect that triethylphosphine will stand higher in the *trans*-influence series than triethylarsine. It is harder to predict the exact position of triethylstibine in the series because ΔS_{Sb} is unexpectedly small compared with ΔS_P and ΔS_{As} and we cannot calculate exactly the heat associated with these entropy effects.

The fact that the dipole moments of *cis*-$(MEt_3)_2PtCl_2$ fall from M = P to M = Sb in spite of increased bond length requires some explanation. Our results indicate that it is not due to greater drift of electrons from the *d*-orbitals of the platinum atom into the *d*-orbitals of the atom M, *i.e.*, stronger π-bonding, so it must be due to weakening of the σ-bond. The classical co-ordinate link should have a bond moment of 4·80 *l* (*l* is the bond length in Å) but the observed value is usually some fraction *x* of this. In the complexes of aluminium and boron, where double bonding cannot occur, *x* is usually less than 0·6 and it appears that as *x* falls the co-ordinate link becomes weaker (Phillips, Hunter, and Sutton, *J.*, 1945, 155). The decrease in dipole moments in spite of greater bond length, *i.e.*, the decreasing *x* in the series of bonds P–Pt, As–Pt, and Sb–Pt, is probably to be associated with the marked parallel weakening of the bonds, for which there is ample qualitative evidence (*e.g.*, see Chatt, *J.*, 1951, 652). This is an effect which need not be associated with double bonding. Our evidence indicates that electron pairs from *d*-orbitals, other than those involved in the symmetrical dsp^2 hybrids, contribute more than 5 kcal. to the strength of the M–Pt bonds; nevertheless, the high dipole moments of the order 10 D., observed for the *cis*-complexes $(MEt_3)_2PtCl_2$, emphasise that the M–Pt bond is in the main a single co-ordinate bond.

Steric Effects.—The platinum atom is so large that steric effects in both *cis*- and *trans*-isomers of the series of complexes $(MEt_3)_2PtCl_2$ (M = P, As, and Sb) are negligible, and can scarcely affect the equilibrium. On the other hand, the nitrogen atom in tertiary amine complexes is sufficiently small to cause considerable strain between the attached hydrocarbon radicals and the adjacent groups on the platinum atom (cf. triethylamine–trimethylborine complexes, Brown *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 1332; 1948, **70**, 2878). There would be more steric strain in the *cis*- than in the *trans*-complexes, but only *trans*-$(NMe_3)_2PtCl_2$ would be reasonably free from steric effects. This steric effect would be an important factor in lowering the stability of $(Et_3N)_2PtCl_2$ and its higher homologues relatively to that of the trimethyl analogue. It cannot be the general explanation of the much lower stability of tertiary amine platinous complexes relatively to their phosphorus

analogues, because even *trans*-$(NMe_3)_2PtCl_2$, where the steric effect is negligible, is unknown.

Instability of Tertiary Amine Complexes.—We consider that two factors are responsible for the very much greater stability of trialkyl-phosphine, -arsine, and -stibine platinous and similar complexes than of their nitrogen analogues: (1) The enhanced strength of the M–Pt bond due to π-bonding between the *d*-orbitals of the atom M and the platinum atom; such bonding is impossible in the N–Pt bond because there are no 2*d*-orbitals. (2) The greater covalent character of the M–Pt than of the N–Pt bond.

The M–Pt bond is in the main a classical co-ordinate bond and it is not likely that the first factor alone will be sufficiently strong to account for the great difference in stability. The second factor is probably important because platinum forms only "inner orbital" complexes (Taube, *Chem. Reviews*, 1952, **50**, 69), in which the ligands are bound by strong covalent bonds. The electronegativities of phosphorus, arsenic, antimony, and platinum are about equal to 2 but that of nitrogen is 3. The much greater electronegativity of nitrogen means that the N–Pt co-ordinate bond will have about 25% ionic character on the basis of Hannay and Smyth's formula (*J. Amer. Chem. Soc.*, 1946, **68**, 171). We should thus have greater dissociation of the N–Pt bond especially in the presence of water, and this would lead to general decomposition of the platinous complex. If, however, the aliphatic tertiary nitrogen atom is part of a multidentate ligand, *e.g.*, $N(CH_2{\cdot}CH_2{\cdot}NH_2)_3$,* which for dimensional reasons fits closely around the metal atom, then the tertiary nitrogen atom is held so that its dissociation from the platinum atom is impossible. In these circumstances, a stable complex with a co-ordinate bond from the tertiary nitrogen to the metal results (Mann and Pope, *Proc. Roy. Soc.*, 1925, *A*, **109**, 444; *J.*, 1926, 482). Monoamines form stable complexes with platinum and similar metals only when the electronegativity of the nitrogen atoms can be reduced. This can occur by neutralisation of the positive charges which develop on complex formation. It takes place either by transmission of the positive charge to hydrogen atoms as in the ammines (Pauling, *J.*, 1948, 1461) or by polarisation of an aromatic system as in pyridine complexes. No mechanism is available to remove the positive charge from the nitrogen atoms of the tertiary alkylamine complexes, and that may be the fundamental cause of their instability. There is no necessity to neutralise the positive charges which develop during the co-ordination of the much less electronegative atoms M, but in fact the first factor above will cause some neutralisation.

Experimental

The triethyl-arsine and -stibine complexes were prepared by the method described in Part III (*loc. cit.*) for the tri-*n*-propyl complexes. They have a greater tendency than their propyl analogues to isomerise spontaneously, so are more difficult to purify. Sharp m. p.s are not good criteria of purity because softening causes isomerisation and immediate melting. The compounds were therefore purified until their *k* values (essentially the same as dielectric constants, see p. 4305) were not altered by further recrystallisation. Five or six rapid recrystallisations from ethanol containing a trace of the bridged $(AsEt_3)_2Pt_2Cl_4$ in the case of the *trans*-isomer, followed by rapid drying at 0·1 mm. after recrystallisation, were sufficient. Our compounds were as follows: *trans*-$(AsEt_3)_2PtCl_2$, m. p. 120—121°; Jensen (*loc. cit.*) reports 120—121°, Nyholm (*J.*, 1950, 843) reports 119°. *cis*-$(AsEt_3)_2PtCl_2$, m. p. 154—155°; Jensen reports 142—142·5°, Nyholm, 142° (Found: C, 24·6; H, 5·1. Calc. for $C_{12}H_{30}As_2Cl_2Pt$: C, 24·4; H, 5·1%); the purification of this compound is best effected by growing large crystals from ethanol solution. *cis*-$(SbEt_3)_2PtCl_2$, m. p. 102·5—103°; Jensen reports 104—104·5°. *trans*-$(SbEt_3)_2PtCl_2$ could not be isolated (compare the propyl analogue, Part III).

The equilibrium concentrations of isomers in benzene were determined by measuring the changes in dielectric constants of benzene solutions of each pure isomer when they were isomerised in the presence of a trace of triethylarsine as catalyst. Isomerisations at temperatures up to 35° were done in the electrical condenser or cell. Those above 35° were carried out in a separate vessel, and the equilibria quenched by the addition of a trace of $(AsEt_3)_2Pt_2Cl_4$ at the higher temperature. The quenched equilibrium mixtures were cooled rapidly, poured into the cell,

* The authors are grateful to the referees for reminding them of this type of exception to the general observation that tertiary alkylamines form only unstable co-ordination compounds with the transition metals.

and their dielectric constants measured at 25°. Triethylarsine and $(AsEt_3)_2Pt_2Cl_4$ were used to catalyse and quench both arsine and stibine equilibria.

The quantities of benzene used in these experiments were those delivered from a particular 50-c.c. graduated flask at the temperature of the dielectric-constant determination; these were, at 15°, 43·81 g.; 20°, 43·58 g.; 25°, 43·36 g.; 30°, 43·14 g.; and 35°, 42·94 g. The increase in electrical capacity of the cell (ΔC) containing mixed solutions of the concentrations we used, over its capacity with pure benzene as dielectric, is given by the equation: $\Delta C = k_c W_c + k_t W_t + k_a W_a$, where W_c = weight of *cis*-isomer, W_t = weight of *trans*-isomer, and W_a = weight of tertiary arsine added to catalyse the isomerisation. The k values are constants for any given substance at any given temperature and were determined by using pure solutions of each component.

cis-$(AsEt_3)_2PtCl_2$ and *cis*-$(SbEt_3)_2PtCl_2$ isomerise spontaneously in benzene solution at room temperature; hence to measure k_c for these substances, a trace (*ca.* 0·2 mg.) of bridged $(AsEt_3)_2Pt_2Cl_4$ was added to their pure solutions. It completely arrested the isomerisation of the arsine complex for sufficient time to allow measurements to be made, and slowed down the isomerisation of the stibine complex sufficiently to permit accurate extrapolation to zero time. The results are recorded in Table 3. W is the total weight of complex used in the experiments, *i.e.*, $W = W_c + W_t$.

The dipole moments of the *cis*-compounds were redetermined at 25° in benzene, the values of ΔC obtained during the determination of the various k_c's being used. This was necessary because Jensen, who required the moments only to determine configuration, made no allowance for spontaneous isomerisation which affects the result appreciably in the case of the stibine complex. The dielectric constant (ε_s) of a solution containing W_c g. of *cis*-complex, of molecular weight M, in 49·33 c.c. of benzene is given by the equation $\varepsilon_s = 1 + 1{\cdot}273(56{\cdot}43 + \Delta C)(56{\cdot}43)^{-}$

TABLE 3

Temp., °K	$10^4/T$	k_c	k_t	W, mg.	W_a, mg.	$\Delta C - k_a W_a$, μμF	W_c, mg.	W_t, mg.	K	log K
Isomerisation of *trans*-$(AsEt_3)_2PtCl_2$										
290·26	34·45	23·05	0·375	1505·1	2·4	0·762	8·7	1496·4	172	2·236
				1858·0	2·4	0·954	11·3	1846·7	164	2·215
				2178·2	2·4	1·109	12·9	2165·3	168	2·225
298·21	33·53	22·63	0·367	2520·3	2·4	1·241	14·2	2506·1	176	2·246
				3018·3	2·4	1·488	17·1	3001·2	176	2·246
308·16	32·45	22·27	0·382	2410·5	2·4	1·208	13·1	2397·4	183	2·262
				2855·9	2·4	1·439	15·9	2840·0	179	2·253
340·4 *	29·38	—	—	3045·5	0·9	1·422	13·7	3031·8	221	2·344
340·7 *	29·35	—	—	2014·0	0·9	0·937	8·9	2005·1	225	2·352
341·5 *	29·28	—	—	2008·6	0·9	0·927	8·5	2000·1	235	2·371
Isomerisation of *cis*-$(AsEt_3)_2PtCl_2$										
298·21	33·53	22·63	0·367	1008·6	5·6	0·495	5·6	1003·0	179	2·253
				1386·8	5·6	0·677	7·6	1373·2	180	2·255
				1503·4	5·6	0·729	8·0	1495·4	187	2·272
341·65 *	29·27	—	—	1000·8	2·8	0·462	4·2	996·6	234	2·369
				1483·4	2·8	0·696	6·8	1476·6	216	2·334
Isomerisation of *cis*-$(SbEt_3)_2PtCl_2$										
290·88	34·38	18·74	0·355 †	196·4	0·3	1·380	71·2	125·2	1·758	0·245
				258·0	0·3	1·822	94·1	163·9	1·742	0·241
298·38	33·51	18·05	0·355 †	254·4	Nil	1·634	87·2	167·2	1·917	0·283
				293·7	Nil	1·898	101·4	192·3	1·896	0·278
				295·0	0·3	1·914	102·3	192·7	1·884	0·275
303·33	32·97	17·63	0·355 †	196·9	0·3	1·168	63·6	133·3	2·096	0·321
				202·5	0·3	1·208	65·8	136·7	2·078	0·318

* In these determinations isomerisation was quenched by addition of a trace of bridged compound (3 mg. or 9 mg.), and the mixture analysed at 25°.

† The values of k_t for the triethylstibine complexes were estimated by extrapolation of the k_t values for the triethyl-phosphine and -arsine complexes.

where the dielectric constant of benzene is assumed to be 2·273 (Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, *A*, **123**, 683) and 56·43 is a cell constant. The dipole moment can then be calculated by using Jensen's approximate formula (*loc. cit.*) which gives the sum of the orientation and atom polarisations ($_0P$ and $_AP$):

$$ {}_0P + {}_AP \simeq \frac{M \times 49{\cdot}33}{W_c}\left(\frac{\varepsilon_s - 1}{\varepsilon_s + 2} - \frac{\varepsilon_B - 1}{\varepsilon_B + 2}\right) $$

In compounds such as these where the total polarisations are of the order 2000 c.c., the atom polarisations can be ignored. Our determinations are listed in Table 4.

TABLE 4

Substance	W_e, g.	ΔC, $\mu\mu$F	ε_s	${}_0P$, c.c.	$\mu = 0{\cdot}2212\sqrt{{}_0P}$, D.	
$(PEt_3)_2PtCl_2$	0·0418	1·112	2·297	2432	10·91	10·9
$M = 502{\cdot}5$	0·0426	1·129	2·298	2424	10·89	
	0·0521	1·376	2·303	2407	10·85	
	0·0540	1·436	2·305	2426	10·89	
$(AsEt_3)_2PtCl_2$	0·0365	0·832	2·291	2455	10·96	10·9
$M = 590{\cdot}3$	0·0376	0·852	2·2915	2433	10·91	
	0·0432	0·967	2·294	2403	10·84	
	0·0590	1·340	2·3025	2433	10·91	
$(SbEt_3)_2PtCl_2$	0·0896	1·630	2·309	2252	10·50	10·45
$M = 684{\cdot}0$	0·0961	1·723	2·311	2219	10·42	
	0·0995	1·792	2·313	2231	10·45	

In the examination of the $(PEt_3)_2PtCl_2$ equilibrium, slightly different values of the equilibrium constant were obtained depending on whether the *cis*- or the *trans*-complex was isomerised (see Part V). In the arsine series, the values obtained by isomerisation of both the *cis*- and the *trans*-complexes are identical within experimental error. The values obtained by isomerisation of the *trans*-complexes have been given most weight because the *cis*-compound is too insoluble in benzene to give sufficient concentration for very accurate measurements. Even in presence of a trace of triethylarsine, 1—1·5 g. of *cis*-isomer required 1—2 hours' vigorous shaking to dissolve it with isomerisation.

Only the *cis*-isomer of $(SbEt_3)_2PtCl_2$ is available, but solubility increases as the series of complexes is ascended from M = P to M = Sb, and in addition more dilute solutions of the stibine complex could be used because the equilibrium lies much farther to the *cis*-side; thus no difficulty was experienced with solubility.

The triethylstibine complex isomerised to give the same equilibrium concentrations whether the isomerisation was spontaneous or catalysed by a trace of triethylarsine. In the former case, equilibrium was reached in about 18 hr. but with the catalyst it was complete in 10 min. The fact that the same equilibrium position was reached under such very different conditions is evidence that the isomerisation is probably free from any important side reactions.

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825. *Synthesis of* 3 : 4- *and* 3 : 5-*Dimethyl Xylose.*

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3 : 5-Dimethyl D-xylose has been synthesised from 3 : 5-*iso*propylidene 2-toluene-*p*-sulphonyl methyl-D-xyloside by methanolysis of the *iso*propylidene residue, followed by methylation and reductive fission of the toluene-*p*-sulphonyl group. Confirmation of a previous synthesis by Robertson and Speedie (*J.*, 1934, 825) of 3 : 4-dimethyl xylose has been obtained by substitution of position 2 by a benzoyl group, in place of the toluene-*p*-sulphonyl residue in the above synthesis, followed by a similar series of reactions. This led to a partial ring change from furanose to pyranose, and to the production of a mixture of dimethyl methylxylosides from which crystalline 3 : 4-dimethyl β-methylxyloside has been isolated.

ISOLATION of 3 : 4-dimethyl xylose from the hydrolysis products of a number of methylated polysaccharides has been reported (Mullan and Percival, *J.*, 1940, 1501; Nelson and Percival, *J.*, 1942, 58; James and Smith, *J.*, 1945, 739), and Robertson and Speedie (*J.*, 1934, 825) have recorded a synthesis based on the blocking of position 2 of the xylose molecule by a benzoyl group and the change of a furanose to a pyranose ring during methanolysis of a 3 : 5-*iso*propylidene residue. In view of the possibility of the migration of the

benzoyl group during methylation, the presumption of ring change, and the fact that there is still some doubt concerning the authenticity of the 3 : 4-dimethyl xylose derived from natural products we considered it advisable to repeat this synthesis and to attempt to characterise the product.

Robertson and Speedie prepared methyl 3 : 5-*iso*propylidene methyl-D-xyloside and blocked position 2 with a benzoyl group. Removal of the *iso*propylidene residue with 1% methanolic hydrogen chloride, followed by methylation, debenzoylation, and hydrolysis gave a syrupy dimethyl methylxyloside. Proof of the structure was based on the isolation of a syrupy dimethyl xylose phenylosazone and recovery of unchanged material after 3 days in cold methanolic hydrogen chloride, indicating that furanoside formation was prevented by the presence of a methoxyl residue on $C_{(4)}$. These authors also converted the dimethyl xylose into the 1 : 2-dibenzoate. Replacement of the benzoyl group at $C_{(1)}$ by bromine followed by methoxyl and removal of the benzoyl group from $C_{(2)}$ gave crystalline 3 : 4-dimethyl β-methyl-D-xyloside.

A synthesis essentially similar to this has now been carried out. By complete conversion of xylose into its methylfuranoside by the method of Levene, Raymond, and Dillon (*J. Biol. Chem.*, 1932, **95**, 699) and substitution of anhydrous copper sulphate for hydrogen chloride during the condensation with acetone, the yield of 3 : 5-*iso*propylidene methyl-xyloside was improved from 17·6 to 70%. In order to avoid the danger of acyl migration the toluene-*p*-sulphonyl residue was used to substitute position 2. This gave crystalline 3 : 5-*iso*propylidene 2-toluene-*p*-sulphonyl methylxyloside (overall yield 41%). Removal of the *iso*propylidene residue by methanolysis followed by methylation and reductive fission of the toluene-*p*-sulphonyl residue gave a syrupy dimethyl methylxyloside. The presence of a furanose ring was indicated by the rate of hydrolysis to the free sugar, the reaction being complete in 0·5 hour with 0·1N-sulphuric acid at 100°. After separation from traces of xylose, monomethyl xylose, and 3 : 4-dimethyl xylose on a cellulose column, the product gave a single spot on a paper chromatogram corresponding to that given by an authentic specimen of 3 : 5-dimethyl xylose kindly supplied by Dr. R. G. Laidlaw. Oxidation of 3 : 5-dimethyl xylose, isolated from the column, with bromine water gave a syrupy lactone, the rate of hydrolysis of which was similar to that quoted by Haworth and Porter (*J.*, 1928, 617) for 3 : 5-dimethyl xylonolactone. Conversion of the 3 : 5-dimethyl xylose into trimethyl methylxyloside, followed by oxidation with nitric acid, esterification, and amide formation gave crystalline 2 : 3-dimethoxysuccindiamide, $[\alpha]_D$ +100° in water. Had Walden inversion occurred on removal of the toluenesulphonyl residue from $C_{(2)}$ the sugar would have been a dimethyl lyxose, which on methylation followed by oxidation would give rise to inactive dimethoxysuccinic acid.

Since only a trace of 3 : 4-dimethyl xylose was formed during this synthesis the presence of the toluenesulphonyl residue on position 2 had clearly prevented ring change during the methanolysis and subsequent methylation. An explanation similar to that advanced by Percival and Percival (*J.*, 1938, 1585) to account for the stability of the glycosidic group in 2 : 4 : 6-trimethyl 3-toluene-*p*-sulphonyl methylgalactoside may be put forward. The close proximity of the toluenesulphonyl residue in the 2 position of the xylose derivatives to the glycosidic hydrogen atom, especially in the β-form, renders the ring completely stable either by mechanical shielding by the large aromatic residue or by formation of a bond between the glycosidic hydrogen atom and the strongly electronegative oxygen atoms of the sulphonyl residue.

Robertson and Speedie's synthesis (*loc. cit.*) was repeated therefore to ascertain the influence of the benzoyl group in the 2-position. The dimethyl methylxyloside prepared in this experiment partly crystallised and the crystals (A) (10·5% of the total yield) were shown to be 3 : 4-dimethyl methylxyloside, by a mixed melting point with an authentic specimen supplied by Dr. J. K. N. Jones. This is in agreement with Robertson and Speedie's results and showed that there had been at least a partial change in ring form from furanose to pyranose. The presence of a pyranose ring in the crystals (A) was proved by the rate of hydrolysis to the dimethyl sugar (see Experimental section). Identity as 3 : 4-dimethyl xylose was confirmed by oxidation with bromine water to crystalline 3 : 4-dimethyl xylonolactone (an authentic specimen was kindly supplied by Dr. J. K. N. Jones).

Complete methylation of the crystals (A) gave crystalline 2 : 3 : 4-trimethyl methylxyloside, and oxidation with nitric acid, esterification, and amide formation gave crystalline inactive *xylo*trimethoxyglutardiamide.

The syrup from which the crystals (A) had been removed was hydrolysed with sulphuric acid and the product separated on a cellulose column into 2 : 3 : 4-trimethyl xylose 22·5%, a mixture of dimethyl xyloses 41%, crystalline 2 : 4-dimethyl xylose 5%, and a mixture of monomethyl xylose and xylose 31·5%. Robertson and Speedie (*loc. cit.*) remarked on the presence of methyl benzoate after treatment with methyl-alcoholic hydrogen chloride and the presence of trimethyl methylxyloside after methylation. Separation of the mixture of dimethyl xyloses on the cellulose column was not successful but analysis by quantitative paper chromatography (Hirst, Hough, and Jones, *J.*, 1949, 928) showed 3 : 5- 26%, 3 : 4- 37%, and 2 : 4-dimethyl xylose 23%, and an unidentified portion 14%.

The mechanism of the reaction is difficult to explain since a number of transformations appear to take place simultaneously. That partial transformation from the furanose to the pyranose ring takes place when the benzoyl group occupies position 2 is shown by the isolation of 3 : 4-dimethyl xylose. The most likely explanation is that this occurs during the removal of the *iso*propylidene group through the influence of the methanolic hydrogen chloride. The reaction is complicated, however, by migration of some of the benzoyl substituent to the 3 position, as shown by the isolation of crystalline 2 : 4-dimethyl xylose. A further complication arises from loss of the benzoyl group and the isolation of considerable quantities of 2 : 3 : 4-trimethyl xylose.

Experimental

3 : 5-iso*Propylidene Methyl*-D-*xyloside*.—Xylose (22 g.) was kept at room temperature with methanolic hydrogen chloride (500 c.c.; 0·5%) until the reducing power had dropped to 5% of the initial value (5 hours) (see Levene, Raymond, and Dillon, *loc. cit.*). Neutralisation with silver carbonate, filtration, and evaporation gave a slightly reducing syrup which after extraction with ethyl acetate and removal of the latter gave a non-reducing syrup (19·2 g.). This was converted into the 3 : 5-*iso*propylidene derivative by Percival and Percival's method (*J.*, 1950, 690). The product was a colourless syrup (B) (22·5 g.) which distilled at 110°/0·1 mm. (21·3 g.), and had n_D^{15} 1·4640, $[\alpha]_D^{15}$ −26° (*c*, 0·6 in water) (Found : $COMe_2$, 30·1. Calc. for $C_9H_{16}O_5$: $COMe_2$, 28·4%).

3 : 5-*Dimethyl* 2-*Toluene*-p-*sulphonyl Methyl*-D-*xyloside*.—To the syrup (B) (21·3 g.) in dry pyridine (60 c.c.) was added powdered toluene-*p*-sulphonyl chloride (29 g.). After 2 days at 15° the mixture was poured on ice, giving a crystalline solid (29·1 g.). Recrystallisation from methanol gave 3 : 5-iso*propylidene* 2-*toluene*-p-*sulphonyl methyl*-D-*xyloside* (19·1 g.), m. p. 120°, $[\alpha]_D^{15}$ −45° (*c*, 0·1 in methanol) (Found : C, 54·4; H, 6·0; S, 9·0. $C_{16}H_{22}O_7S$ requires C, 53·6; H, 6·2; S, 8·95%). Treatment of this substance (19·10 g.) with methanolic hydrogen chloride (100 c.c.; 1%) at 70° for 1 hour gave 2-*toluene*-p-*sulphonyl methylxylofuranoside* as a yellow syrup (16·9 g.), n_D^{15} 1·5269, $[\alpha]_D^{15}$ +41° (*c*, 1·2 in methanol). This substance (16·5 g.) was then methylated 3 times with methyl iodide and silver oxide, giving a pale yellow syrup (17·9 g.), n_D^{15} 1·5025. Solution in light petroleum (b. p. 60—80°) (100 c.c.) and extraction with water (4 × 10 c.c.) removed any fully methylated xyloside. After drying (Na_2SO_4), the light petroleum was evaporated, leaving 3 : 5-*dimethyl* 2-*toluene*-p-*sulphonyl methyl*-D-*xyloside* as a colourless oil (C) (15·5 g.), n_D^{18} 1·5061 (Found : OMe, 26·45. $C_{15}H_{22}O_7S$ requires OMe, 26·9%).

3 : 5-*Dimethyl Methylxyloside*.—The substance (C) (15·4 g.) in methanol (300 c.c.)–water (80 c.c.) was reduced with sodium amalgam (150 g.; 4%) with stirring at 35° during 16 hours. After filtration and repeated extraction with chloroform the chloroform extracts were neutralised with carbon dioxide, dried (Na_2SO_4), and evaporated under diminished pressure. Extraction of the residue with ethyl acetate and removal of the solvent gave a syrup which on distillation gave : Fraction 1 (4·3 g.), b. p. 105—115°/0·01 mm., n_D 1·4500 (Found : OMe, 49·3. Calc. for $C_8H_{16}O_5$: OMe, 48·4%), shown to consist of 3 : 5-dimethyl xylose very slightly contaminated with xylose, monomethyl xylose, and 3 : 4-dimethyl xylose; fraction 2 (2·3 g.), b. p. 115—130°/0·01 mm., n_D 1·4553 (Found : OMe, 26·2%), which was purified by extraction with ethyl acetate from aqueous solution. Redistillation at 105—115°/0·1 mm. gave a colourless syrup (1·1 g.), n_D^{15} 1·4512 (Found : OMe, 47·9%).

Characterisation of 3 : 5-*Dimethyl Xylose*.—The 3 : 5-dimethyl methylxyloside (138 mg.), $[\alpha]_D^{15}$ + 102° (*c*, 1·39 in water), was hydrolysed at 100° with 0·1N-sulphuric acid (11 c.c.) until

the rotation ($[\alpha]_D^{15}$ +17·5°) was constant (0·5 hour). After neutralisation of the solution with barium carbonate and evaporation to dryness 3 : 5-dimethyl xylose was obtained as a colourless syrup. This was separated from traces of 3 : 4-dimethyl xylose, monomethyl xylose, and xylose on a column of powdered cellulose (Chanda, Hirst, and Percival, *J.*, 1951, 1240). The solvent employed for elution was purified light petroleum (b. p. 100—120°)–*n*-butanol (6 : 4) saturated with water. A colourless syrup was obtained, having n_D 1·4583, $[\alpha]_D$ +23° (*c*, 1·3 in water), +10° (*c*, 1·3 in chloroform). Laidlaw (*J.*, 1952, 2942) reports +25° (*c*, 1·13 in water), +11° (*c*, 0·84 in chloroform). Attempts to prepare a crystalline anilide were unsuccessful, with the exception of once when a minute quantity of crystals, m. p. 126—127°, was obtained. The sugar (0·8 g.) was oxidised to the lactone (0·7 g.), b. p. 110—125°/0·08 mm., $[\alpha]_D$ +75° (4 minutes), +82° (24 minutes), +72° (24 hours), +67° (7 days), +56° (11 days), +27° (33 days, constant) (*c*, 1·34 in water) (cf. Laidlaw, *loc. cit.*; Haworth and Porter, *loc. cit.*; Levene and Raymond, *J. Biol. Chem.*, 1933, **102**, 331).

3 : 5-Dimethyl methylxyloside (0·8 g.) was methylated 3 times with methyl iodide and silver oxide, and a colourless syrup (2 : 3 : 5-trimethyl methylxylose) (0·8 g.) was isolated. This had n_D^{15} 1·4431, $[\alpha]_D^{15}$ +114° (*c*, 0·1 in methanol), +134° (*c*, 0·33 in water) (Found : OMe, 60·6. Calc. for $C_9H_{18}O_6$: OMe, 60·3%). This syrup (0·7 g.) in nitric acid (10 c.c.; *d* 1·4) was heated at 50° until the evolution of brown fumes had ceased (2 hours). The solution was then kept at 95° for 6 hours. The acid was removed by continuous addition and removal of water under diminished pressure. The syrup (0·420 g.) so obtained was esterified by methanolic hydrogen chloride (10 c.c.; 2%) for 6 hours at 65°. After neutralisation and evaporation of the solvent distillation gave a syrupy ester (0·25 g.), b. p. 120—130°/0·1 mm., n_D^{15} 1·4370, $[\alpha]_D^{15}$ +52° (*c*, 0·1 in methanol). Treatment of this ester for 2 days at 0° with methanol (10 c.c.) saturated with ammonia gave crystals of 2 : 3-dimethoxysuccindiamide (18 mg.), m. p. 270° (decomp.), unchanged on admixture with an authentic specimen, $[\alpha]_D$ +100° (*c*, 0·31 in water) (Found : OMe, 35·5; N, 16·2. Calc. for $C_6H_{12}O_4N_2$: OMe, 35·2, N, 15·9%).

2-*Benzoyl* 3 : 4-*Dimethyl Methylxyloside.*—3 : 5-*iso*Propylidene methylxyloside (6·4 g.) was treated with benzoyl chloride by Robertson and Speedie's method (*loc. cit.*). The product was a syrup (8·8 g., 94·5%) which partly crystallised at 0°. The crystals (2-benzoyl 3 : 5-*iso*propylidene methylxyloside) (1·2 g.) had m. p. 86°, $[\alpha]_D^{15}$ +114° (*c*, 0·1 in chloroform) (Found : C, 62·3; H, 6·5; $COMe_2$, 18·65. Calc. for $C_{16}H_{19}O_6$: C, 62·5; H, 6·2; $COMe_2$, 18·8%). A mixture of syrup and crystals (7·6 g.) when treated with methanolic hydrogen chloride as described for the 2-toluenesulphonyl derivative gave a syrup (6·6 g.), n_D 1·5217, $[\alpha]_D^{15}$ +31° (*c*, 1·3 in chloroform) (Found : OMe, 16·15. Calc. for $C_{13}H_{16}O_6$: OMe, 11·6%), which after 3 methylations with silver oxide and methyl iodide gave a pale yellow syrup (6·4 g.). Solution of the latter in benzene and extraction with water (4 × 25 c.c.) partly removed trimethyl methylxyloside. The purified material (5·2 g., 71%) was debenzoylated by Zemplén's method (*Ber.*, 1929, **62**, 1613), giving a colourless syrup (D) (2·3 g., 68%) which partly crystallised. The crystals (needles; 0·25 g.) were separated and after recrystallisation from light petroleum (b. p. 60—80°) had m. p. 88—89°, not depressed by an authentic specimen of 3 : 4-dimethyl methylxyloside supplied by Dr. J. K. N. Jones (Found : C, 49·9; H, 8·3; OMe, 48·5. Calc. for $C_8H_{16}O_5$: C, 50·0; H, 8·4; OMe, 48·45%), $[\alpha]_D^{15}$ −33° (*c*, 2·48 in chloroform), −58° (*c*, 0·47 in water). Robertson and Speedie recorded m. p. 89—90°, $[\alpha]_D$ −82·5° (*c*, 2·0 in chloroform), for 3 : 4-dimethyl β-methylxyloside.

Characterisation of 3 : 4-*Dimethyl Xylose.*—Crystalline 3 : 4-dimethyl methylxyloside (47 mg.), $[\alpha]_D^{15}$ −58° (*c*, 0·47 in water), was hydrolysed with 0·1N-sulphuric acid at 100° for 6·5 hours, by which time the rotation had changed to $[\alpha]_D^{15}$ +22°. After a further 40 minutes' heating with N-sulphuric acid the rotation was $[\alpha]_D^{15}$ +35° (constant). After neutralisation and evaporation of the solvent 3 : 4-dimethyl xylose was obtained as a colourless syrup (35 mg.). This was oxidised by bromine water in the usual way. The product which distilled at 125—135°/0·03 mm. solidified on cooling and was obtained on recrystallisation from light petroleum (b. p. 60—80°) as large needles, m. p. 68°, unchanged on admixture with an authentic sample of 3 : 4-dimethyl xylonolactone.

Crystalline 3 : 4-dimethyl methylxyloside (250 mg.) when twice treated with methyl iodide and silver oxide gave crystalline 2 : 3 : 4-trimethyl methylxyloside which after purification by sublimation (yield 106 mg.) had m. p. 44—45°, $[\alpha]_D^{15}$ −46° (*c*, 1·0 in chloroform). This substance (106 mg.) was oxidised with nitric acid as described previously. Esterification of the product with methanolic hydrogen chloride followed by amide formation with methanolic ammonia gave crystalline *xylo*trimethoxyglutardiamide, m. p. 197°, alone or on admixture with an authentic specimen, $[\alpha]_D$ 0° (*c*, 0·5 in water).

Examination of the Syrup (D).—Hydrolysis of the syrup (D), after removal of the crystalline 3 : 4-dimethyl methylxyloside, with N-sulphuric acid at 100° until the rotation was constant ($[\alpha]_D$ +36°), and examination of the product on a paper chromatogram revealed the presence of trimethyl xylose (R_G 0·94), 3 : 5- (R_G 0·52), 3 : 4- (R_G 0·42), and 2 : 4-dimethyl xylose (R_G 0·39), an unidentified sugar (R_G 0·30), and some monomethyl xylose and xylose. This mixture (1·06 g.) was separated on a column of powdered cellulose (Chanda, Hirst, and Percival, *loc. cit.*). The solvent employed for elution was purified light petroleum (b. p. 100—120°)–*n*-butanol (1 : 1) saturated with water. Fraction 1 (0·260 g.) was trimethyl xylose, n_D 1·4560. Fraction 2 (0·423 g.) was a mixture of 3 : 5-, 3 : 4-, and 2 : 4-dimethyl xylose. Fraction 3 (0·052 g.) was crystalline 2 : 4-dimethyl xylose, m. p. 110°. Fraction 4 (0·32 g.) was a mixture of monomethyl xylose and xylose. Quantitative determination of the dimethyl sugars in fraction 2 by the method of Hirst, Hough, and Jones (*loc. cit.*) with benzene–amyl alcohol–ethanol–water (1·7 : 1 : 1 : 0·25) as the eluting solvent indicated the presence of 3 : 5-dimethyl xylose 26%, 3 : 4-dimethyl xylose 37%, 2 : 4-dimethyl xylose 23%, and an unidentified sugar (R_G 0·30) 14·5%.

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KING'S BUILDINGS, UNIVERSITY OF EDINBURGH. [*Received, July 18th,* 1952.]

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826. *Structural and Stereochemical Correlation of Metanethole with Other Dimerides of Aryl Propenyl Compounds.*

By WILSON BAKER, C. N. HAKSAR, J. F. W. MCOMIE, and T. L. V. ULBRICHT.

Metanethole (II) reacts with acetyl chloride and aluminium chloride to give a dihydroxy-diketone (IV), which is oxidised by alkaline hydrogen peroxide to a tetrahydric phenol (III; R = R′ = H). Methylation of the latter gives the known dimeride of *iso*eugenol methyl ether (III; R = R′ = Me). The saturated dimerides of 4-methoxy-, 4-hydroxy-3-methoxy-, 3 : 4-dimethoxy-, 4-ethoxy-3-methoxy-, 3 : 4-dibenzyloxy-, and (probably) 3-hydroxy-4-methoxy- and 3 : 4-methylenedioxy-propenylbenzenes are all now known to be derived from the one stereoisomeride of 1-ethyl-2-methyl-3-phenylindane.

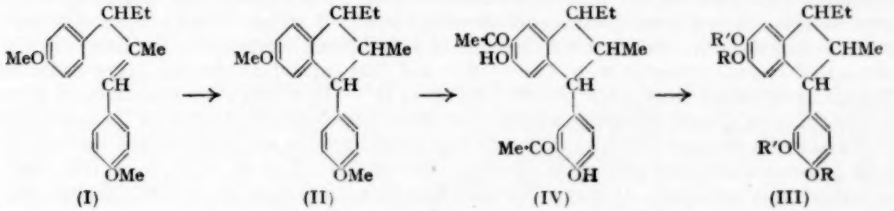
AROMATIC propenyl compounds, *e.g.*, anethole, *p*-MeO·C_6H_4·CH:CHMe, sometimes occur naturally, but are usually obtained from the allyl isomerides, *e.g.*, eugenol and safrole, by treatment with alkali. They give stable dimerides under the influence of acid reagents, and the first of these substances whose structure was established was an unsaturated dimeride of anethole, *iso*anethole, which was proved by Goodall and Haworth (*J.*, 1930, 2482) to possess structure (I); *cis*- and *trans*-forms of *iso*anethole have been obtained by Baker and Flemons (*J.*, 1948, 1984). Pailer (*Monatsh.*, 1947, **77**, 45) showed that a dimeric liquid form of *iso*safrole (3 : 4-methylenedioxypropenylbenzene) possesses a structure similar to that of *iso*anethole (I).

The more commonly formed dimeric propenyl compounds are saturated, *e.g.*, metanethole, di*iso*eugenol, and the dimeride of *iso*eugenol methyl ether, and these substances were for long thought to be derivatives of either *cyclo*butane or 9 : 10-dihydroanthracene.* It was shown first by Baker and Enderby (*J.*, 1940, 1094) that metanethole was, beyond reasonable doubt, 1-ethyl-5-methoxy-2-methyl-3-*p*-methoxyphenylindane (II), and subsequent investigations mainly by A. Müller and his collaborators (*Ber.*, 1942, **75**, 692, 891; 1943, **76**, 855, 1061, 1119; 1944, **77**, 6, 12, 159, 325, 343; *J. Org. Chem.*, 1947, **12**, 815; 1951, **16**, 481, 1003; van der Zanden and de Vries, *Rec. Trav. chim.*, 1949, **68**, 261, 407) have provided additional evidence of the accuracy of this formula. Attempted stepwise

* The only established case of this type appears to be 9 : 10-diethyl-9 : 10-dihydro-2 : 3 : 6 : 7-tetramethoxyanthracene obtained in 0·07% yield by dimerisation of *iso*eugenol methyl ether (Pailer, *loc. cit.*).

synthesis of metanethole involving final catalytic reduction of 1-ethyl-5-methoxy-3-*p*-methoxyphenyl-2-methylindene gave a stereoisomer of (II) (four racemates are possible), m. p. 99° (metanethole, m. p. 135°) (van der Zanden and de Vries, *loc. cit.*; A. Müller, Toldy, Halmi, and Mészáros, *J. Org. Chem.*, 1951, **16**, 481), but reduction of the indene with sodium and ethanol gave metanethole itself, m. p. 134—134·5° (van der Zanden and de Vries, *Rec. Trav. chim.*, 1952, **71**, 733). The simultaneous production of *iso*anethole (I) and metanethole from the ketone MeO·C_6H_4·CHEt·CHMe·CO·C_6H_4·OMe by treatment with aluminium *iso*propoxide (A. Müller, Toldy, Halmi, and Mészáros, *loc. cit.*) does not provide proof of the structure of metanethole, as it may have been formed *via iso*anethole; the change *iso*anethole to metanethole has been effected by stannic chloride (Baker and Enderby, *loc. cit.*), aluminium chloride, and titanium tetrachloride (A. Müller, Mészáros, Lempert-Sréter, and Szára, *J. Org. Chem.*, 1951, **16**, 1003) and it may take place slowly at room temperature, probably under the influence of traces of acid (Polak and Hixon, *J. Amer. Pharm. Assoc.*, 1945, **34**, 240; Baker, unpublished observation). Again, the metanethole isolated from a species of sponge by Bergmann and McAleer (*J. Amer. Chem. Soc.*, 1951, **73**, 4969) may be an artifact derived from anethole.

Di*iso*eugenol and its dimethyl ether (di*iso*homogenol) are now known to be phenylindanes (III; R = H, R′ = Me; and R = R′ = Me, respectively) analogous to metanethole (A. Müller and Horváth, *Ber.*, 1943, **76**, 855; Cartwright and Haworth, *J.*, 1947, 1094; von Doering and Berson, *J. Amer. Chem. Soc.*, 1950, **72**, 1118), the identity of the fundamental structures being proved by the fact that the dimethyl ether of di*iso*eugenol is identical with the dimeride of *iso*eugenol methyl ether (Haworth and Mavin, *J.*, 1931, 1363; Kovács, *J. Org. Chem.*, 1950, **15**, 15). The same structure (III; RR′ = CH_2) has been established beyond reasonable doubt by Pailer (*loc. cit.*; Pailer, U. Müller, and Porschinski, *Monatsh.*, 1948, **79**, 620) for the solid dimerides of *iso*safrole [m. p.s 95° and 146°; these are possibly dimorphic forms as the former was stated to be converted into the latter at 150° (Mayer, *Atti R. Accad. Lincei*, 1914, **231**, 358), although we have been unable to confirm this observation], and Pailer, U. Müller, and Porschinski



(*loc. cit.*) have also obtained a partial correlation between the di*iso*safrole, m. p. 146°, and di*iso*eugenol dimethyl ether by degrading them both to the same 1-ethyl-5 : 6-dihydroxy-2-methylindane. Moreover, we have been able to oxidise the lower-melting di*iso*safrole to 2-methyl-5 : 6-methylenedioxy-3-(3 : 4-methylenedioxyphenyl)inden-1-one, a compound previously obtained (Pailer, Müller, and Porschinski, *loc. cit.*) by similar oxidation of the higher-melting di*iso*safrole, thus providing strong evidence that the two di*iso*safroles are either dimorphic or stereoisomeric forms. Stepwise syntheses of the indane (III; R = R′ = Me) (by A. Müller and Gál, *Ber.*, 1944, **77**, 343; A. Müller, Toldy, Halmi, and Mészáros, *loc. cit.*; Cartwright and Haworth, *J.*, 1947, 948; Horning and Parker, *J. Amer. Chem. Soc.*, 1952, **74**, 3870) gave products differing slightly in melting point from di*iso*eugenol dimethyl ether, of which they were regarded as stereoisomerides (mixed m.p.s showed depressions).

It is probable that dimerisation of aryl propenyl derivatives to give saturated compounds will give in all cases the same stereoisomeride of 1-ethyl-2-methyl-3-phenylindane (as II) bearing the appropriate nuclear substituents. It therefore became of importance to attempt the conversion of metanethole (II) into di*iso*eugenol dimethyl ether (dimeride of eugenol methyl ether; di*iso*homogenol) (III; R = R′ = Me) by introducing two methoxyl groups into the molecule, and this has now been achieved in the following manner.

Metanethole reacted with acetyl chloride in ether in presence of a very large excess of aluminium chloride (conditions critical) to give a diphenolic diketone, 6-acetyl-3-(3-acetyl-4-hydroxyphenyl)-1-ethyl-5-hydroxy-2-methylindane (IV) arising by a double Friedel–Crafts reaction and simultaneous demethylation (cf. reaction of acetyl chloride–ether upon 1 : 2 : 3 : 5-tetramethoxybenzene and upon pentamethoxybenzene, Baker, *J.*, 1941, 662). When less aluminium chloride was used 6(?)-acetylmetanethole was isolated. Reaction of the diketone (IV) with alkaline hydrogen peroxide (Dakin reaction) gave the tetrahydric phenol, 1-ethyl-5 : 6-dihydroxy-3-(3 : 4-dihydroxyphenyl)-2-methylindane (III; R = R′ = H), which was easily oxidised and could not be successfully purified. When treated with methyl sulphate and alkali, this phenol gave its tetramethyl ether, 1-ethyl-5 : 6-dimethoxy-3-(3 : 4-dimethoxyphenyl)-2-methylindane (III; R = R′ = Me), m. p. 94—96°, undepressed when mixed with an authentic specimen of di*iso*eugenol dimethyl ether, m. p. 95—96°; the identity was further proved by *X*-ray powder photographs, which showed exact correspondence of all lines (over twenty) in both position and intensity. It has not previously been clearly recognised that this racemic di*iso*eugenol dimethyl ether is dimorphic. Slow crystallisation from methanol gives a product, m. p. 105-106°; the m. p. falls after several weeks to 95-96°, and this lower-melting form is also obtained by rapid crystallisation from concentrated solutions (see Experimental; A. Müller, Mészáros, Körmendy, and Kucsman, *J. Org. Chem.*, 1952, **17**, 787; Ciamician and Silber, *Atti R. Accad. Lincei*, 1909, **18**, 1216).

Attempts to extend this correlation to di*iso*safrole by small-scale methylenation of the tetrahydric phenol (III; R = R′ = H) derived from metanethole did not succeed. In order to render the tetrahydric phenol (III; R = R′ = H) more available we unsuccessfully attempted, under a variety of conditions, both the demethylation of di*iso*eugenol and the demethylenation of di*iso*safrole, and finally reinvestigated a substance, supposed to be (III; R = R′ = H) (Kovács, *loc. cit.*). Kovács dimerised 3 : 4-dibenzyloxypropenylbenzene by treating its dibromide with sodium iodide in acetone, and reduced the dimeride catalytically to remove the benzyl groups; the crude product (not obtained solid or analysed) was then treated with diazomethane, giving a substance (not analysed), m. p. 106°, which differed from di*iso*eugenol dimethyl ether, of which it was supposed to be a stereoisomeride. We find that the dimeride of 3 : 4-dibenzyloxypropenylbenzene has m. p. 104—105° (Kovács records m. p. 114—116°), and that catalytic reduction gives either (*a*) the uncharacterised tetrahydric phenol (III; R = R′ = H) which with diazomethane gives a dimorphic compound indistinguishable from di*iso*eugenol dimethyl ether, or (*b*) unchanged material and a product which has lost only two benzyl groups and which when methylated with diazomethane gives a dibenzyl dimethyl ether of (III; R = R′ = H), m. p. 103—105°, of unknown orientation. It is possible that Kovács's compound, m. p. 106° (above), may have been this dibenzyl dimethyl ether of (III; R = R′ = H).

Two further correlations between dimeric arylpropenyl compounds may be noted. (1) A. Müller, Toldy, Halmi, and Mészáros (*loc. cit.*) showed that the diethyl ether of di*iso*eugenol is identical with the dimeride of 4-ethoxy-3-methoxypropenylbenzene obtained from 4-ethoxy-3-methoxy-α-methylcinnamic acid by heating it with sulphuric acid (cf. *p*-methoxy-α-methylcinnamic acid which is similarly converted into metanethole and also *iso*anethole, Baker and Enderby, *loc. cit.*; these reactions undoubtedly proceed by loss of carbon dioxide followed by dimerisation of the propenyl compound). (2) The saturated dimeride of 3-hydroxy-4-methoxypropenylbenzene (*iso*chavibetol) gives a dimethyl ether which exists in two forms, m. p. 94—96° and 105·5—106·5° [Funakubo, Kawasaki, and Hoshimoto, *J. Chem. Soc. Japan*, 1941, **63**, 1555 (see *Chem. Abs.*, 1947, **41**, 3442)] and is without doubt identical with di*iso*eugenol methyl ether (also dimorphic, see above), although it is not known if mixed melting points were carried out.

To summarise, it has now been established (with possibility of slight doubt in cases marked with *) that the saturated dimerides of the following aryl propenyl compounds are all derived from the one stereoisomeride of 1-ethyl-2-methyl-3-phenylindane: 4-methoxypropenylbenzene (anethole), 3 : 4-dimethoxypropenylbenzene (*iso*eugenol methyl ether), and 3 : 4-dibenzyloxypropenylbenzene (this paper); 4-hydroxy-3-methoxypropenylbenzene (*iso*eugenol) (Haworth and Mavin; Kovács); 4-ethoxy-3-methoxypropenylbenzene

(A. Müller, Toldy, Halmi, and Mészáros); 3-hydroxy-4-methoxypropenylbenzene* (Funakubo, Kawasaki, and Hoshimoto); 3 : 4-methylenedioxypropenylbenzene* (*iso*safrole) (Pailer, U. Müller, and Porschinski). The parent substance, 1-ethyl-2-methyl-3-phenylindane, is with little doubt the compound " methronol " (for references, etc., see Baker and Enderby, *loc. cit.*) obtained by decarboxylation and dimerisation of α-methylcinnamic acid under the influence of sulphuric acid (see above); it yields benzoylbenzoic acid on oxidation.

Saturated dimerides of other arylethylene derivatives are, in addition, known to be substituted phenylindanes, *e.g.*, dimeric styrene (Spoerri and Rosen, *J. Amer. Chem. Soc.*, 1950, **72**, 4918) and dimeric *p-iso*propenyltoluene (Hukki, *Acta Chem. Scand.*, 1945, **3**, 279) (for a summary of earlier work on dimerides of substituted ethylenes, see Bergmann and Weiss, *Annalen*, 1930, **480**, 49).

Experimental

M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

6-Acetyl-3-(3-acetyl-4-hydroxyphenyl)-1-ethyl-5-hydroxy-2-methylindane (IV) *and 6(?)-Acetylmetanethole.*—Anhydrous ether (100 c.c.) was added slowly, with cooling in ice, to anhydrous aluminium chloride (137 g., 50 mols.). Metanethole (Baker and Enderby, *loc. cit.*) (6 g., 1 mol.) was then added in portions to the viscous solution followed by the dropwise addition of redistilled acetyl chloride (8·0 c.c., 5·6 mols.). After being stirred for 1 hour the mixture was heated at 50—60° for 2 hours, the dark red product poured into ice (400 g.) and concentrated hydrochloric acid (150 c.c.), and after being heated for 1 hour on the water-bath the liquid was extracted with ether (2 × 200 c.c.). The extracts (see * below) were shaken with 10% aqueous sodium hydroxide (100 c.c.), the alkaline layer acidified with dilute hydrochloric acid, and the liberated oil taken up in ether (200 c.c.). The dried ethereal extract yielded an oil which later solidified, and was crystallised 3 times from ethanol (charcoal). This *6-acetyl-3-(3-acetyl-4-hydroxyphenyl)-1-ethyl-5-hydroxy-2-methylindane* (IV) formed needles, m. p. 115—116° (1·0—2·5 g., 15—35%) (Found : C, 75·3; H, 6·9. $C_{22}H_{24}O_4$ requires C, 75·0 ; H, 6·8%). It gives a purple colour with alcoholic ferric chloride. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol–ethyl acetate in minute, red needles, m. p. 260° (decomp.) (Found : N, 15·5. $C_{34}H_{32}O_{10}N_8$ requires N, 15·7%).

The yield of the diketoindane (IV) is apt to vary considerably in this preparation. When the amount of aluminium chloride was reduced to 20 mols., a non-phenolic product was isolated from the ethereal solution (* above) as an oil which slowly solidified. This was crystallised three times from ethanol (charcoal), giving *6(?)-acetylmetanethole* as colourless needles, m. p. 122° (1·2 g.) (Found : C, 78·0; H, 7·6. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol–ethyl acetate as an orange-red, microcrystalline powder, m. p. 225° (decomp.) (Found : N, 11·2. $C_{28}H_{30}O_6N_4$ requires N, 10·8%).

1-Ethyl-5 : 6-dihydroxy-3-(3 : 4-dihydroxyphenyl)-2-methylindane (III; R = R′ = H).—Aqueous hydrogen peroxide (3%; 30 c.c., 3 mols.) was added to a solution of the diketone (IV) (3 g.) in N-sodium hydroxide (67·5 c.c., 6 mols.) in an atmosphere of nitrogen. The temperature rose from 19° to 36° in ½ hour, and the yellow solution became deep red. After a further 2 hours, the mixture was kept at about 50° for 10 minutes, then cooled, and a little sodium dithionite (hydrosulphite) added to decolorise the solution, which was then poured into water (200 c.c.) and acidified with dilute sulphuric acid. After ½ hour, the solid was collected, washed, and dried (yield 2·4 g.; m. p. 90—105°). This tetrahydroxy-compound could not be satisfactorily recrystallised and did not yield a crystalline tetra-acetate.

Diisoeugenol Dimethyl Ether (III; R = R′ = Me).—(*a*) *From the tetrahydroxy-compound* (III; R = R′ = H). Aqueous sodium hydroxide (20%; 10 c.c., 6 mols.) was slowly added to a stirred solution of the crude tetrahydroxy-compound (2·4 g.) in methanol (15 c.c.) and methyl sulphate (5 c.c., *ca.* 7 mols.) in an atmosphere of nitrogen, and the vigorous reaction was moderated by cooling in water. Similar quantities of methyl sulphate and alkali were then added alternately in portions, and the mixture was finally heated on a water-bath for 3 hours. The solution, made slightly alkaline, was extracted with ether (200 c.c.), and the extract washed with water, dried (K_2CO_3), and distilled, leaving a brown oil which solidified. Crystallisation from methanol (charcoal) yielded di*iso*eugenol dimethyl ether as microcrystalline needles (0·12 g.), m. p. 85—90°, raised to 94—96° by 3 further crystallisations from methanol. A mixed m. p.

with an authentic specimen of di*iso*eugenol dimethyl ether (m. p. 95—96°) was undepressed, and with the polymorphic form (m. p. 105—106°; see next two paragraphs) the mixed m. p. was 103—104° (Found: C, 74·2; H, 7·7; OMe, 34·5. Calc. for $C_{22}H_{28}O_4$: C, 74·2; H, 7·9; OMe, 34·8%).

(*b*) *From di*isoeugenol. Methylation of di*iso*eugenol (Haworth and Mavin, *J.*, 1931, 1364) with methyl sulphate and sodium hydroxide gave, after crystallisation from methanol, di*iso*eugenol dimethyl ether, m. p. 105—106°. After several weeks the material had m. p. 95—96°. Slow recrystallisation from a dilute solution in methanol gave the higher-melting form, whereas concentrated solutions deposited the lower-melting form; thus the two forms are clearly polymorphic modifications.

(*c*) *From* 3 : 4-*dibenzyloxypropenylbenzene*. A mixture of the dibromide of 3 : 4-dibenzyloxypropenylbenzene (3·8 g.; Kovács, *loc. cit.*) and sodium iodide (3 g.) in pure, dry acetone (30 c.c.) was kept for 9 days, a solution of sodium thiosulphate (4·2 g.) in water (160 c.c.) added, and the solid collected and crystallised from ethanol, giving 5 : 6-dibenzyloxy-3-(3 : 4-dibenzyloxyphenyl)-1-ethyl-2-methylindane (III; R = R′ = CH_2Ph) (0·9 g., 70%), m. p. 101—103°, raised by further recrystallisation to 104—105° (Kovács gives m. p. 114—116°, and yield 33%) (Found: C, 83·5; H, 6·4. Calc. for $C_{46}H_{44}O_4$: C, 83·7; H, 6·7%). Palladium black (0·1 g.), suspended in ethanol (5 c.c.), was saturated with hydrogen, a solution of the tetrabenzyl ether (0·2 g.) in absolute ethanol (100 c.c.) added, and the mixture shaken in hydrogen (1 atm.) till uptake of hydrogen ceased. The filtered solution was treated with excess of diazomethane, and yielded a product which separated from methanol in crystals, m. p. 93—95° (rapid heating). When heated slowly it partially melted at 93—95°, then solidified, and remelted at 104—105°. The same behaviour was shown on admixture with di*iso*eugenol dimethyl ether.

Dibenzyl Dimethyl Ether of 1-*Ethyl*-5 : 6-*dihydroxy*-3-(3 : 4-*dihydroxyphenyl*)-2-*methylindane*. —When the reduction of the benzyl ether (III; R = R′ = CH_2Ph) was carried out in presence of one-fifth of the amount of catalyst previously used, and the product treated with diazomethane as above, unchanged starting material (0·2 g.) was recovered, together with a solid *ether* (0·1 g.), m. p. 103—105° after crystallisation from methanol (Found: C, 80·9; H, 6·5. $C_{34}H_{36}O_4$ requires C, 80·3; H, 7·1%).

*Oxidation of Di*isosafrole, *m. p.* 95°. 2-*Methyl*-5 : 6-*methylenedioxy*-3-(3 : 4-*methylenedioxyphenyl*)*inden*-1-*one*.—Chromic acid (3·5 g.) in water (5 c.c.) and acetic acid (25 c.c.) was added (½ hour) to a stirred, cooled solution of di*iso*safrole (m. p. 95°; 5 g.) in acetic acid (100 c.c.). After 2 hours, benzene (15 c.c.) and light petroleum (35 c.c.; b. p. 60—80°) were added, and next day stirring was continued for 4 hours, water added, and the mixture extracted with benzene. The extract, after being washed with alkali and water, was distilled, and the residue sublimed several times at 170—190°/0·4 mm., and finally crystallised from ethanol, giving 2-methyl-5 : 6-methylenedioxy-3-(3 : 4-methylenedioxyphenyl)inden-1-one as red plates, m. p. 229—231° (Found: C, 70·4; H, 3·9. Calc. for $C_{18}H_{12}O_5$: C, 70·1; H, 3·9%) (Pailer, Müller, and Porschinski, *loc. cit.*, record m. p. 231—232°). The compound gave a reddish-brown 2 : 4-*dinitrophenylhydrazone*, m. p. 288—290° (decomp.), which crystallised from benzene–alcohol (Found: N, 11·0. $C_{24}H_{16}O_8N_4$ requires N, 11·5%).

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827. *Some Aspects of the Solution Chemistry of Zirconium.*

By B. A. J. Lister and (Miss) L. A. McDonald.

Some experiments are described dealing with the chemistry of zirconium in nitric, hydrochloric, perchloric, and sulphuric acid solutions. Ion-exchange techniques have been used to determine the ionic charge of zirconium species and the degree of cation–anion interaction to form complex cations, and to illustrate the presence of anionic complexes in solution. In addition, the rate of diffusion from solution into exchangers of different degrees of cross-linking has given information on ionic size at various acidities. Other experiments include the measurement of the rate of self-diffusion in solution, electromigration studies, and pH determinations.

The results are interpreted as indicating the presence at lower acid concentrations of polynuclear hydrolysis products, and at higher acidities of such complexes as (in nitric acid solution) $[Zr(NO_3)_2(H_2O)_4]^{2+}$, $[Zr(OH)_2(NO_3)(H_2O)_3]^{+}$, $[Zr(OH)_2(NO_3)_2(H_2O)_2]^{2+}$, and $[Zr(OH)_2(NO_3)_4]^{2-}$.

Great differences are apparent between the behaviour of ionic species of zirconium and thorium in comparable solutions.

Little is known with certainty of the individual zirconium species existing in aqueous solutions and there is lack of agreement on the composition of materials crystallised from solution. An outstanding feature in the chemistry of zirconium in solution is the large degree of hydrolysis, and although claims have been made to have established the existence of the normal nitrate, it is generally agreed that normal salts of quadrivalent zirconium are never crystallised. A short survey of this early work has been made by one of us [Lister, Thesis, London, 1951; A.E.R.E. C/R 801 (1951)].

Several important papers have recently been published, notably those by Connick and McVey (*J. Amer. Chem. Soc.*, 1949, **71**, 3182), Connick and Reas (*ibid.*, 1951, **73**, 1171), and Larsen and Gammill (*ibid.*, 1950, **72**, 3615). Connick *et al.* used a new technique in examining the behaviour of α-trifluoro-α′-thenoylacetone (TTA) for zirconium complexes under different conditions. The degree of anion–cation interaction was examined by Connick and McVey by studying the TTA extraction coefficient as a function of the concentration of complex-forming ion at constant hydrogen-ion concentration and diketone activity. Their results were taken to indicate the presence in 1—2N-nitric and -hydrochloric acid solution of one NO_3^- or Cl^- ion in the respective complexes. Later work by McVey (Hanford Works Report 21,487) has shown the presence of the first and second nitrato-complexes, $ZrNO_3^{3+}$ and $Zr(NO_3)_2^{2+}$ in nitric acid solutions up to 4M.

Connick and Reas examined the hydrolysis of zirconium in perchloric acid solution by similar extraction methods and concluded that formation of polynuclear ions occurs even at 2N-acidity. They quote details of polymerisation under different conditions of zirconium and perchloric acid concentration. A claim is also made that, at very low concentrations of zirconium in 2N-perchloric acid, the zirconium monomer is mainly present as Zr^{4+} although at lower acidities the presence of $Zr(OH)^{3+}$ and $Zr(OH)_2^{2+}$ has been indicated. McVey has also observed the presence of the latter ion and has, by optical-density measurements, confirmed some of the polymerisation data of Connick and Reas.

A study of the titration curves of zirconium and hafnium in perchloric, nitric, and hydrochloric acid solution by Larsen and Gammill (*loc. cit.*) led to some interesting results. For perchlorate solutions, over three quarters of the precipitation range, the logarithm of the hydroxyl-ion concentration was shown to be a linear function of the metal-ion concentration and, from the slope of the curve, the average charge for the ion in solution was shown to be 0·6 and the average number of hydroxyl ions per zirconium atom to be 3·4. This was taken to mean that polymeric species existing in solution over this range had the average composition $[M(OH)_{3\cdot4}^{0\cdot6+}]_n$. Significant differences were found in the behaviour of zirconium and hafnium in nitrate and chloride solution.

Objects of Present Work.—It was hoped that use of a number of different physicochemical techniques would afford additional information on the state of zirconium in solu-

tion, and that further checks might be made of the recent extraction work described above. The experiments now detailed fall under several headings : (*a*) examination of ionic complexity by measurements of the rate of self-diffusion in solution and of the rate of diffusion into ion-exchange resins, (*b*) determination of ionic charge by an ion-exchange technique, (*c*) examination of the degree of cation–anion interaction to form complex cations, and of the presence of zirconium in anionic form, ion-exchange methods being used in both series of experiments, (*d*) electromigration studies, and (*e*) pH measurement on zirconyl salt solutions. Attention has been confined to perchloric, nitric, hydrochloric and, in some cases, sulphuric acid solutions.

It should be stressed that in the ion-exchange experiments the relative accumulation of the species in the resin phase is not identical with that in the solution phase owing to variations in ionic size as well as to the fact that species of higher charge are generally more strongly held in the resin phase than those of lower charge. However, valuable information has been obtained by examination of the resin phase after equilibration with the solution.

In the experiments now described, two cation-exchange materials have been used, Zeokarb 225 and Dowex 50, both sulphonated polystyrene resins cross-linked by addition of about 10% of divinylbenzene. [The properties of such resins are described by Reichenberg, Pepper, and McCauley (*J.*, 1951, 493) and by Topp and Pepper (*J.*, 1949, 3299).]

Experimental

(1) *Rate of Self-diffusion in Solution.*—The diffusion coefficients of zirconium species in solutions of various acidities were measured by Jander and Jahr (*Koll. Beih.*, 1936, **43**, 295) who found a fall in the rate of diffusion with decrease in acidity, their results being in agreement with the formation of highly aggregated hydrolysis products. It was also suggested that the progress of hydrolysis may differ markedly with the anion present, and that nitric acid and perchloric acid solutions of zirconium hydroxide differ fundamentally in their chemical properties.

The availability of radio-isotopes has made it possible, in contrast to previous work, to determine self-diffusion in solution, *i.e.*, diffusion under conditions where there exists no concentration gradient. Anderson and Saddington (*J.*, 1949, 5381) have described measurements of self-diffusion coefficients of tungstic acids, and their technique has been closely followed in the present work. Briefly, it entails measurement of the rate of diffusion of the ion concerned from an active solution contained in a capillary cell into an external solution of the same composition but with no added radio-tracer.

To interpret our results, the expression $\gamma = 8e^{-\theta}/\pi^2$, derived from Fick's law, has been used. In this expression γ = fraction of activity remaining in the capillary cell, and $\theta = \pi^2 Dt/4L^2$, where D = diffusion coefficient at the temperature of the experiment (29·6°), t = time of diffusion, and L = length of capillary cell.

The solutions used were all 1% in zirconyl nitrate (*ca.* 0·04M), the nitric acid concentration varying from 0·02 to 6M. Radioactive tracers for these and other experiments were prepared by irradiating hafnium-free zirconyl nitrate [the hafnium being removed by a cation-exchange technique (Lister, *J.*, 1951, 3123)] in the Harwell pile for 4 weeks. The weak β-activity due to the zirconium daughter-product, niobium, was removed by counting through a 20 mg./cm.^{2} aluminium filter.

The results are shown in Fig. 1. The scatter may be due to the unavoidably low counting rate and to possible small differences in the preparation of the solution which might affect the complexity of the ions.

A complete theoretical treatment of the relation between diffusion coefficient in liquid systems and ionic or molecular weight is lacking. As an approximation, Riecke's relationship (*Z. phys. Chem.*, 1890, **6**, 564) (the molecular weight is considered as inversely proportional to the square of the diffusion coefficient) may be used to evaluate the results; it then appears that between solutions of zirconium in 0·02M- and 6M-nitric acid there is an approximately six-fold decrease in the weight of the ionic species. Jander and Jahr found wide differences in the values of the diffusion coefficient with the interval between preparation of the solution and measurement. After 2—7 weeks they found that, over the range 0·5—3 moles of acid per mole of zirconium salt, the product of the diffusion coefficient and the specific viscosity varied from 1·5 to 1·8. After 10·5 months these values had changed to 1·0—1·8. The first figures represent a factor of 1·45 in the molecular weight at the two acidities, and the latter figures a factor of 3·2. In the present work, over this same range (*ca.* 0·02—0·12M-acid), a factor of 2·1 was found. The

results are not directly comparable since Jander and Jahr carried out their experiments in the presence of a large excess of a second electrolyte; however, the general trend is the same.

The present results give no evidence of any one ionic species predominating over any range of acidity, but show, instead, a gradual change in molecular weight (the experimentally determined diffusion coefficients representing an average value).

(2) *Rate of Ion Exchange of Zirconium Cations from Nitric Acid Solution.*—If zirconium species of varying complexity and ionic size are present in solutions of different acidity, then these differences should be reflected in the rate at which the species will be taken up by an ion-exchange resin. The method chosen for this study was one in which the degree of reaction was determined *in situ* without separation of resin and solution, measurements being made continuously by means of a radio-tracer technique.

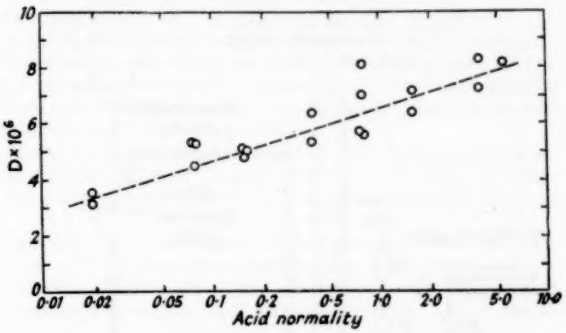


FIG. 1. *Self-diffusion coefficients of zirconium species in nitric acid solution.*

The apparatus is shown in Fig. 2. A known volume of the solution under examination (seeded with radioactive tracer-^{95}Zr) was admitted to the apparatus at *A* by means of a plunger pipette. A constant-pressure air stream was injected at point *B via* a mercury bubbler and a series of needle valves, and the solution was caused to circulate round the apparatus by air rising in tube *C*. The apparatus was built in 0·2-mm. diameter Pyrex capillary tubing with the exception of the reaction cup *D* and the lead-shielded Geiger–Müller tube *E*. In all experiments the solution contained 300 mg. of zirconium nitrate seeded with hafnium-free active material in 30 ml. of nitric acid. The solution in the reaction cup was gently stirred with a constant slow-speed motor and glass stirrer. After addition of 1 g. of oven-dried resin (Zeokarb 225 in the hydrogen form) to the reaction cup, the uptake of zirconium from the solution was measured by observing the counting rate of the solution passing through the flow counter. A small time lag must occur between the reaction and observation of the change in activity, but, as a constant circulation rate of about 25 ml./minute was maintained, this time lag was only important during the first few minutes of the run and a small correction could be applied. The large vertical separation of the reaction cup and Geiger–Müller tube (*ca.* 100 cm.) was necessary to ensure that radiation from the zirconium absorbed on the resin did not affect the observed counting rate of the solution. In addition, the circulation rate is dependent on the vertical distance between the air-injection point and the reaction cup.

The rate of exchange must vary with the pore size of the resin, *i.e.*, with the degree of cross-linking. To examine this effect, two resins were used, the normal production material with 10% of divinylbenzene and a specially prepared resin of similar composition but with only 5% of divinylbenzene and, consequently, a much more open structure.

The results now obtained with zirconium all show that particle diffusion is the controlling mechanism as distinct from film diffusion (Kressman and Kitchener, *Discuss. Faraday Soc.*, 1940, **7**, 90), linear relationships being found between Q_t/Q_∞ and $\sqrt{t}$ at low values of Q_t/Q_∞, where Q_0 = original amount of solute, Q_t = amount taken up at time t, Q_∞ = amount taken up at equilibrium, r = radius of the resin particle, and D = diffusion coefficient.

The determination of Q_∞ presented some difficulty with solutions of lower acidity. In such solutions, a relatively rapid uptake over the first hours was followed by a flattening of the uptake curve to a value which rose extremely slowly, in some cases over weeks. In difficult cases this initial plateau level has been taken as the value of Q_∞. This final very slow uptake may be ascribed to either a resin or a solution effect, *i.e.*, it may arise from a slow permeation of the large ions into the resin structure or to a slow continuous readjustment of equilibrium in solution to

produce ions which can exchange more readily. The latter appears more likely since pH measurements have shown a continuous slow change in the hydrogen-ion concentration over many days.

For comparison purposes one run was made with a simpler ion. Thorium was chosen since its uptake has been shown (Kressman and Kitchener, *loc. cit.*) to obey a $\sqrt{t}$ law and the same expression

$$Q_t/Q_\infty = 6Q_0\sqrt{Dt/\pi}/r(Q_0 - Q_\infty)$$

could be used to calculate the diffusion coefficient. The rate of uptake with a solution of thorium nitrate in water (no added acid) was over ten times that in any of the zirconium runs ($D \sim 4 \times 10^{-8}$), indicating a simpler ionic structure.

FIG. 2. *Air-lift apparatus for determining rates of exchange.*

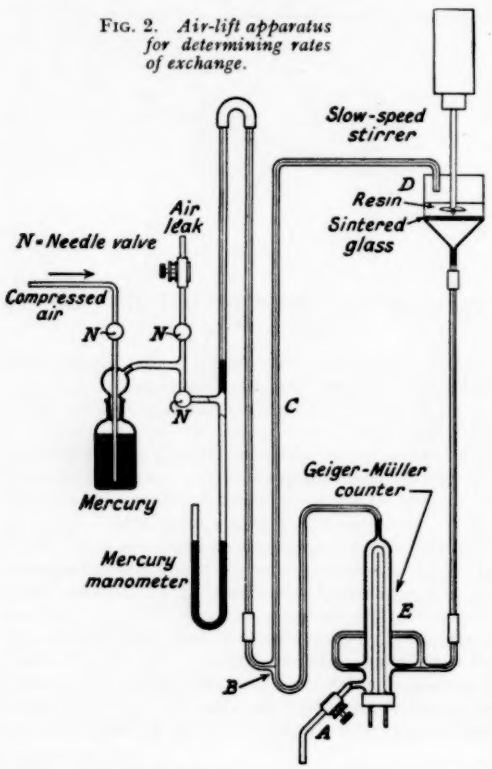
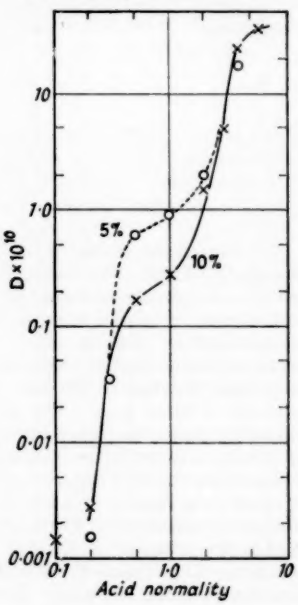


FIG. 3. *Resin diffusion coefficients of zirconium species as function of acid normality and degree of resin cross-linking.*



The results obtained for zirconium are shown in Fig. 3. It is seen that the diffusion coefficient falls away very rapidly with decreasing acidity, this being in agreement with the formation of highly aggregated hydrolysis products. These aggregates appear to be formed even in quite strongly acid solutions. The shape of the curves is interesting and may be explained qualitatively by the following simplified picture. At a limiting acid concentration somewhere above 6N we can suppose that simple ionic species only are present with a certain high mean diffusion coefficient. As we decrease the acidity, larger polynuclear species appear, causing a drop in the average value of D. If no further aggregation occurred we should expect the curve to level out at a value corresponding to the mean diffusion coefficient of these polynuclear ions. Before this state is reached, however, the formation of still more highly aggregated species causes another rapid drop in the diffusion coefficient.

Differences in the curves obtained with 5% and 10% divinylbenzene resins are most marked over the region of 0·3—3·0 acid normality, and it is presumably in this region that the ionic species present are comparable in size with the resin pores. At higher acid concentrations the

smaller ions can diffuse into either resin with equal ease and at lower acidities both 5% and 10% cross-linked materials have a close enough structure to prevent substantially the diffusion of the larger ions present. A figure of 4—6 Å has been quoted by Kressman (private communication) for the pore size of the 10% cross-linked resin. Thus the simplest zirconium species (*i.e.*, ZrO^{2+} — bond length *ca.* 2·3 Å) would have easy access to the exchange sites, whereas a polymeric ion of the type $(O{=}Zr{-}O{-}Zr{=}O)^{2+}$ with a major diameter of about 8—10 Å would be hindered.

The method, then, as well as giving a qualitative description of the state of the solution with varying acidity, gives a semi-quantitative picture of the ionic size of the species. An important factor which cannot be evaluated is the size of the water sheath associated with the zirconium species and its effect in determining the rate of diffusion of the ion through the resin.

The fact that a stepwise curve is obtained in this series of experiments while a smooth relation is found between acidity and rate of self-diffusion in solution is explained by the sieve-like action exhibited by the cross-linked resin structure.

(3) *Cation–Anion Interaction to Form Complex Cations.*—Interaction of zirconium-containing cations with the anion of the acid solvent to produce complex cations has been proposed by a number of investigators working with different acid solutions, but most of the previous work has resulted in theories that fit the experimental data rather than in unambiguously proved facts, and the nature of the complex cations in solution is still far from certain.

The use of ion-exchange resins seemed to offer a method whereby the combination of an acid anion in the zirconium cationic species could be demonstrated and, at least, a semi-quantitative description given of the variation in the nature of this complex cation with the acid solvent and the acid concentration.

Let us suppose in a solution of a zirconium salt in an acid, HX, there exists the complex cation $[Zr(OH)_pX_m]^{n+}$ where $m + p = 4 - n$. If this is absorbed on to a resin anion we have formed a resinate $R_n[Zr(OH)_pX_m]$. From a knowledge of the general ease of hydrolysis of zirconium ions we could expect, on washing this zirconium resinate with water, either of the reactions

(*a*) $R_n[Zr(OH)_pX_m] + (m + n)H_2O = Zr(OH)_4 + mHX + nRH$
(*b*) $R_n[Zr(OH)_pX_m] + mH_2O = R_n[Zr(OH)_{(p+m)}] + mHX$

Of these two reactions the second is the more likely and this is confirmed by the ease of removal by complex-forming agents of the zirconium species from a water-washed resin and the general similarity in behaviour of washed and unwashed zirconium resins to elution with acids. Further experiments have shown that the zirconium species are in fact in an ionised form after being washed with water and we can confidently ignore reaction (*a*). That hydrolysis does occur on washing, was confirmed by showing that a surface-dried and water-washed sample of resin which had been equilibrated with a hydrochloric acid solution of zirconium nitrate released no chloride ion on regeneration with oxalic acid, which strongly complexes the zirconium.

Hence, water-washing of a resin with absorbed zirconium species, say, $[Zr(OH)_2X]^+$, yields hydrogen ions formed by the hydrolysis of group X according to the equation $R[Zr(OH)_2X]^+ + H_2O = R[Zr(OH)_3]^+ + HX$. The amount of acid released gives a direct measure of the amount of hydrolysable groups on the resin. This can then be compared with the weight of zirconium on the resin and an average value found for the ratio $\overline{X}/\overline{Zr}$ (where the bars refer to the resin phase).

The technique adopted was as follows. A 5-g. sample of oven-dried Dowex 50 in the hydrogen form was shaken with a solution of 2 g. of zirconyl nitrate in 200 ml. of a solution of known acid strength (1—6N). After 24 hours the liquor was separated by suction through a funnel, and the resin surface-dried by rubbing with filter-paper until a freely mobile material was obtained. Experience made this condition quite easy to reproduce. The resin was transferred to a small column and washed with 250 ml. of water, and the acidity of the washings was determined by titration with 0·1N-sodium hydroxide solution (bromothymol-blue). The zirconium held on the resin was removed by elution with oxalic acid solution or 3N-sulphuric acid and determined as oxide.

When a resin is shaken with an electrolyte solution, some of the solution goes into the pores of the resin without the ions being exchanged. This, of course, is also removed on water-washing and in each case a control experiment had to be made with an acid solution containing no zirconium. The difference between the acidity found from washing the mixed zirconium–hydrogen resin and that from the control experiment gave a measure of the hydrolysable groups present on the mixed resin. The quantitative nature of the results may be affected by probably small differences in electrolyte uptake between the pure hydrogen form and the mixed hydrogen–

zirconium form of the resin, but this was minimised by keeping the zirconium–hydrogen ratio on the resin small. The experimental results are shown in Figs. 4 and 5.

With perchloric acid solutions very little excess of hydrogen ion is produced on water-washing, the small amount actually found possibly being due to differences in the electrolyte uptake over a range of zirconium concentrations on the resin. It is therefore clear that there is little, if any, cation–anion interaction to give complex cations in perchloric acid solutions. With nitric and hydrochloric acid solutions, however, the results show a gradual rise in the amount of cation–anion interaction with increasing acid concentration. The curves for these two acids are similar up to a concentration of 3N, but above this the amount of interaction in nitric acid solution increases more rapidly than in hydrochloric acid solution reaching, at 6N, a ratio $\overline{NO_3}:\overline{Zr} = 1:1$. The average formula for the species absorbed from 3N-acids appears to be $[Zr(OH)_{3\cdot84-n}X_{0\cdot16}]^{n+}$, and from 6N-acids $[Zr(OH)_{(3-n)}NO_3]^{n+}$ or $[Zr(OH)_{(3\cdot5-n)}Cl_{0\cdot5}]^{n+}$. It must be remembered that this method examines only the species absorbed on the resin and not directly those in solution, although the results are a reflection of the state of the solution.

An interesting fact arises from the curves of Fig. 5. The equilibrium uptake of zirconium from acid solution varies greatly with the nature of the acid, perchloric acid allowing a much larger uptake than either nitric or hydrochloric acid. In fact, in 5N-solution there is less than

Fig. 4. *$\overline{X}/\overline{Zr}$ ratio for species absorbed on resin from various acid solutions.*

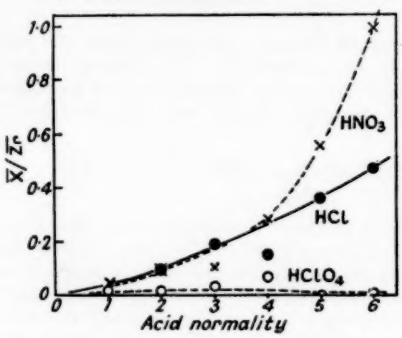
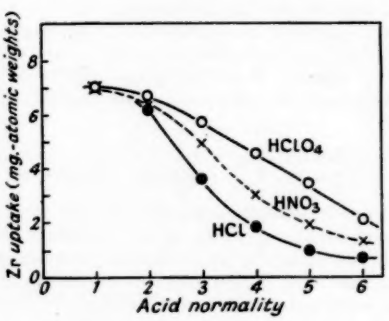


Fig. 5. *Resin uptake of zirconium from various acid solutions after 24 hrs.' contact.*



one-third of the uptake from hydrochloric acid solution that occurs with perchloric acid. Examination of the activity coefficients of the three acids at high concentrations shows a reason for the discrepancy between the behaviour in nitric acid and in hydrochloric acid solutions, the activity coefficients of the former being far lower than those of the latter. This reasoning is not, however, valid when considering perchloric acid since the activity coefficients of perchloric acid are the highest of the three. An explanation must therefore be sought in the possibility of the presence of anionic complexes or undissociated molecules, or a difference in ionic charge.

To examine the effect of increase of nitrate concentration at constant acidity, a series of experiments was carried out similar to those described above but with the nitric acid concentration kept at 1N, and the nitrate-ion concentration increased by addition of lithium nitrate. The results obtained under the two sets of conditions are compared in Table 1.

Table 1. *Dependence of $\overline{NO_3}/\overline{Zr}$ on nitrate concentration.*

Nitrate concn. (N)	1	2	3	4
$\overline{NO_3}/\overline{Zr}$ (HNO_3 only)	0·051	0·088	0·109	0·286
$\overline{NO_3}/\overline{Zr}$ (1N-HNO_3 + $LiNO_3$)	0·051	0·045	0·043	0·065

It is apparent from these figures that an increase in nitrate concentration without an increase in acidity does not affect the $\overline{NO_3}/\overline{Zr}$ ratio of the cations absorbed on the resin. Hence, any further nitration of the ionic species must yield either uncharged molecules or anionic species. The zirconium uptake after 24 hours' contact was similar in both series of experiments.

These results are further discussed on p. 4326.

(4) *The Presence of Zirconium in Anionic Form.*—To obtain an indication of the presence of

zirconium in complex anionic form, the degree of uptake from solution on an anion-exchange resin was examined. 2-G. samples of air-dried highly basic resin (De-acidite FF) were shaken for 24 hours with 25 ml. of solutions of different acidity containing 1·0 g. of zirconium nitrate seeded with radioactive hafnium-free zirconium tracer. The resin and solution were separated, and the activity of the final solution was compared with that of the original solution by counting 5-ml. samples contained in a glass cell centred beneath a Geiger–Müller tube. Three separate portions of each solution were counted in this way. The results obtained are collected in Table 2.

TABLE 2. *Uptake of zirconium by anion-exchange resin.*

Acid	N	Uptake, %	Uptake (1N-HNO_3 + $LiNO_3$), %	Acid	N	Uptake, %	Uptake (1N-HNO_3 + $LiNO_3$), %
$HClO_4$	2	4·3	—	HNO_3	2	0 *	0 *
	4	0·9 *	—		4	2·0 *	0 *
	6	1·1 *	—		6	10·2	8·9
HCl	2	0 *	—	H_2SO_4	0·5	57·5	—
	4	5·3	—		1·0	21·5	—
	6	8·1	—		1·5	10·0	—

* Within statistical deviations.

In assessing the results certain facts should be considered. The stability of the anion exchanger to solutions of high ionic strength and particularly of high acidity must always be in doubt, although De-acidite FF is claimed to be one of the most stable anion exchangers. Depression of the uptake by total anion concentration is marked as shown by figures obtained with sulphuric acid solutions. Although it is known from other results that the amount of zirconium existing in anionic form in solution increases with the concentration of sulphuric acid, the present work has shown a rapid decrease in uptake as the acid concentration is raised from 0·5 to 1·5N.

Thus the method is probably of limited value in a quantitative assessment of the complex anion content of the solution, particularly as our knowledge of the reactions of anionic resins is more limited than is the case with cationic resins. Nevertheless, the results with hydrochloric and nitric acid solutions indicate strongly that, at the higher acidities, some zirconium does exist as anionic complexes.

An explanation of the results with perchloric acid (lower uptake with higher acidity) can be found in the probability of resin decomposition in the presence of more concentrated perchloric acid. The resin was, in fact, greatly darkened in 4N- and 6N-perchloric acid solutions, whereas no change was noticed in the appearance of the resin in contact with other acids.

Results from comparable experiments with mixtures of nitric acid (1N) and lithium nitrate to a total nitrate concentration of 2—6N show no significant differences (Table 2).

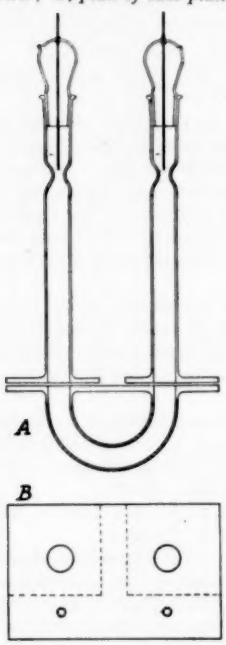
(5) *Electromigration Experiments.*—To obtain further information on the existence of anionic complexes of zirconium and the degree to which such complex-formation occurs, experiments were made on the electromigration of zirconium species in different acid solutions. An apparatus was constructed similar to that made by Coehn (*Ber.*, 1902, **35**, 2676) and used by Ruer (*Z. anorg. Chem.*, 1904, **42**, 94) when studying zirconium solutions. It was essentially a Pyrex glass U-tube so designed that the catholyte, anolyte, and central solution could be separated without the need for constrictions at stopcocks where local heating would arise. As illustrated in Fig. 6, the anolyte and catholyte sections (diameter *ca.* 0·8 cm.) were mounted in ground-glass Pyrex plates which, with the aid of a thin layer of lubricant, were able to slide smoothly over a third ground-glass plate (9 × 6 cm.) carrying the central U-shaped section. Thus each section of the apparatus could be filled separately and brought into contact at the start of the experiment with very little disturbance of the boundary. The electrodes were platinum wires of *ca.* 1 mm. diameter held in position in ground-glass joints containing a small hole for the escape of gas. They were immersed about 1 cm. in the solution which was filled to a mark on the upper part of the vessel. The electrode compartments held *ca.* 4 ml. of liquid and the central compartment *ca.* 8 ml. At the end of the run, the two electrode compartments were again separated from the central section and were emptied by sliding them over two vertical exit tubes sealed into the base plate as shown in Fig. 6 (*B*).

In all the work described, the zirconyl nitrate used (previously freed from hafnium impurity) had been pile-irradiated so that the migration could be followed radiochemically. The central compartment was filled initially with a solution containing 100 mg. of activated zirconyl nitrate per 10 ml. of solution of given acidity, and the electrode compartments with the same acid solution but no zirconium. Aliquots of the original and final central solutions and the final anolyte and

catholyte were counted by using standard β-counting equipment. A control run was carried out under identical conditions but with no current, so that a correction for diffusion across the boundary could be applied in each case. The current used in all runs was 40 ma., and the time of electrolysis 2 hours. Other experiments (to be published later) have shown that the amount of anode-directed migration is not a linear function of time.

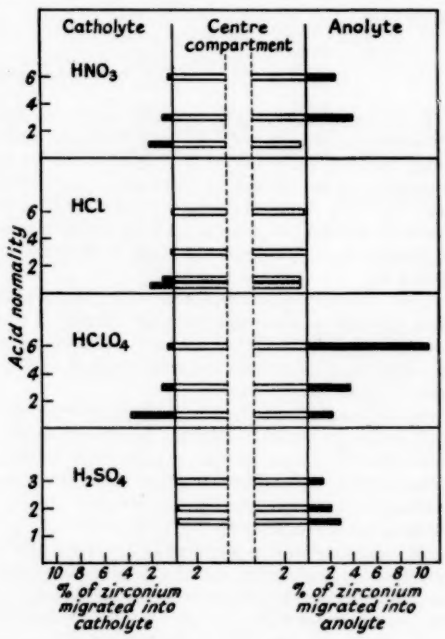
The results obtained with solutions in perchloric, hydrochloric, nitric, and sulphuric acids are shown in Fig. 7. The percentage migration to the two compartments shown pictorially has been corrected for diffusion. In some cases the amount of zirconium transferred in the diffusion control experiment was slightly greater than that found in the comparable run during electrolysis, *i.e.*, the diffusion into, say, the cathode compartment has been overcome by electromigration

FIG. 6. U-*Tube apparatus for electromigration experiments*: *A, side view*; *B, plan of base plate.*



Note.—Marks on stems of apparatus near electrodes are marks to which apparatus is filled with solution.

FIG. 7. *Results of* U-*tube electromigration experiments.*



towards the anode. This is shown in the diagram by a retraction of the migration line back into the central compartment. As the acid strength increases, competition with the acid anion will result in less transference of zirconium for the same amount of the same zirconium ions in solution.

Perchloric acid solution. A very pronounced anion migration was observed even in 1N-solution. This anode-directed movement increased considerably with increase in acidity, the amount of zirconium moving towards the cathode decreasing correspondingly.

Nitric acid solution. In 1N-solution only cation migration was noted, but at the higher acidities there was very marked movement of zirconium towards the anode, the somewhat smaller migration at 6N possibly being accounted for by hydrogen-ion competition. The cation migration gradually decreased with rise in acidity.

Hydrochloric acid solution. Very little movement of zirconium in either direction was found. At 0·5N- and 1N-acidities definite migration to the cathode occurred but at higher acid concentrations the increase in zirconium concentration found in the catholyte and anolyte was within experimental error (<0·2%).

Sulphuric acid solution. As expected, considerable anion transference was found, this decreasing with rise in acidity between 1·5 and 3N, presumably owing to sulphate-ion competition (cf. results of section 4).

The two most striking features of this series of experiments are the apparent lack of migration in hydrochloric acid solutions and the large anion transference in perchloric acid solutions. The experiments are direct ones and considerable reliance can be placed on them. The only similar experiments on record are those of Ruer, who used 2% solutions of zirconyl chloride in 0·5N- and saturated hydrochloric acid and in 0·5N-sulphuric acid. In the first solution he found considerable cathode-directed migration of zirconium and negligible movement to the anode, in agreement with the present results. The movement in saturated acid solution was considerably less to the cathode but rather more to the anode. Ruer's measurements of small migrations must, however, be less precise than the present results using radio-tracer methods. Unfortunately, there is little comparison of migrations in other acids, the only other quoted result being a twenty-fold larger migration to the anode than to the cathode in 0·5N-sulphuric acid.

The present results can be explained on the basis of complex equilibrium systems involving the presence in solution of cations, anions, and uncharged molecules. These results are correlated with those obtained by other methods on p. 4326.

(6) *Determination of Ionic Charge of Zirconium Cationic Species.*—The general scheme followed in the present work was an equilibration of a batch of cation-exchange resin with the solution under investigation, and determination of the weight uptake of zirconium by gravimetric means, and of the equivalent uptake of zirconium species on the resin. A full investigation into methods and technique was carried out with the system zirconyl nitrate–nitric acid and the major part of the work described in this section deals with this system.

0·5-G. samples of Dowex 50 in the hydrogen form were shaken with solutions of 0·25 g. of zirconyl nitrate in 25 ml. of nitric acid solution varying in concentration from 0·1 to 6·0N. After a given time interval the resin was transferred to a small column (1 cm. in diameter) and supported on a sintered-glass disc. The weight of zirconium held on the resin was found by precipitating the hydroxide from the original and final solutions with ammonium hydroxide, drying it, igniting it to the oxide in silica crucibles, and weighing it.

The resin in the mixed zirconium–hydrogen form was washed with water till the washings were neutral to litmus solution, and then about 100 ml. of N-sodium chloride solution were allowed slowly to percolate through the resin bed. The hydrogen ions liberated from the resin by sodium ions were determined by titration with 0·1N-sodium hydroxide (bromothymol-blue). The zirconium on the column was removed with 0·5% oxalic acid solution, and the resin treated with N-sulphuric acid to reconvert it into the hydrogen form. After being washed with water to remove excess of acid, the column was again eluted with N-sodium chloride solution, the acidity of the eluate being a measure of the total equivalent capacity of the resin sample. The difference between the two alkali titration values gave the number of resin equivalents occupied by the zirconium ions.

The effect of washing a resin in the zirconium form with water has been considered in Section 3. Further experiments have shown that less than 20 p.p.m. of zirconium are removed from the resin by such treatment.

If a is the number of mg.-atoms of zirconium taken up by the resin (from gravimetric data), e the number of m.-equiv. of resin occupied by the zirconium, and n the number of zirconium atoms in the ionic species, then the number of complex ions on the resin $= a/n$, and the charge on the complex ion $= V_c = en/a$. If $e/a = V_s$, the measured quantity, from now on called the mean specific ionic charge, then $V_c = nV_s$. It is clear that by this method the charge on a polynuclear ion can only be found if the number of zirconium atoms in the polymer is known.

The values found for V_s are shown graphically in Fig. 8. For simplicity, only the mean values of many determinations are shown. The results obtained with solutions between 2N and 6N in nitric acid could be explained on the basis of a simple equilibrium, involving mononuclear species,

$$[Zr(OH)_m(NO_3)_{(3-m)}]^{3+} + H_2O \rightleftharpoons [Zr(OH)_{(m+1)}(NO_3)_{(3-m)}]^{+} + H^+$$

or, more generally, $[ZrA]^{3+} \rightleftharpoons [ZrB]^{+} + H^+$. The values for V_s move in the expected direction, *i.e.*, a higher ionic charge in more concentrated acid solutions. Below 2N-acid, however, the V_s values behave abnormally, a sharp increase being noted with increasing acid dilution. The results in this region are far less easily reproducible, suggesting that some less rigid secondary process is becoming operative.

This rapid rise in specific charge can only be explained if some sort of steric effect is assumed at the lower acidities. It is suggested that at acidities below 2N, there are formed large polynuclear hydrolysis products, and that these complexes when absorbed on the resin tend to block some of the pores (which in this class of resin are, on the average, of the order of 4—6 Å in diameter). This blocking effect prevents the eluting sodium ions from reaching some of the hydrogen sites and thus the hydrogen-ion concentration found in the sodium chloride eluate is too small. The equivalent zirconium concentration on the resin thus appears too high, and with it the value of V_s. This supposition is supported by a series of experiments carried out with solutions of varying zirconium concentration but constant acidity (Fig. 9). Further evidence in support of this is a reduction in the value of V_s when a 5% cross-linked resin is used (Fig. 8). Although this reduction could certainly be caused by a smaller degree of pore blocking, yet it

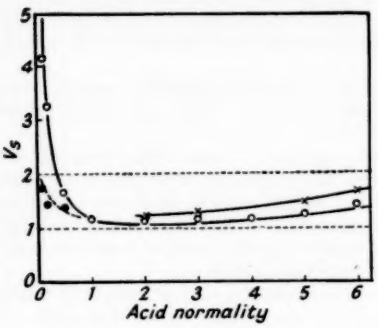


FIG. 8. *Variation of V_s with acid normality (mean experimental values) showing effect of resin cross-linking.*

○ *Nitric acid*; 10% *cross-linked resin.*
● *Nitric acid*; 5% *cross-linked resin.*
× *Perchloric acid*; 10% *cross-linked resin.*

FIG. 9. *Effect of zirconium concentration on value of V_s for nitric acid solutions.*

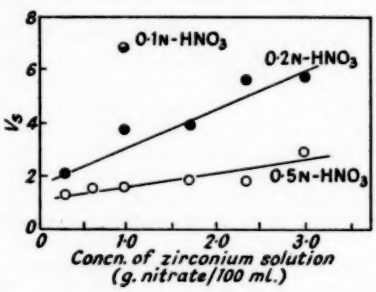
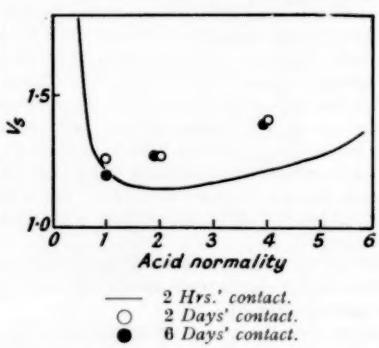


FIG. 10. *Effect of contact time on value of V_s for nitric acid solutions.*



could equally arise by a relatively greater uptake of polynuclear ions when the specific charge is unity or less.

Further to test the blocking mechanism theory, experiments were made to determine the mean specific ionic charge in solutions of ammonium chloride and tetraethylammonium iodide (major diameter 7·2 Å). Although the results tend to confirm the theory, ions of larger diameter would have to be used for a complete test.

Several methods have been tried to avoid the difficulty of resin blocking at low acidities, all of them based on a complete regeneration of the mixed zirconium–hydrogen resin (*e.g.*, with oxalic acid and sodium and ammonium oxalate solutions), and examination of the eluate from the regeneration. In no case, however, were useful results obtained.

The work described in Section 2 showed the rate of uptake of zirconium from solution to be slow. The effect of this slow exchange on the value of V_s was examined. Similar experiments were performed with solutions in 1N-, 2N-, and 4N-acid after contact times of 2 hours, 2 days, and 6 days. The results (Fig. 10) show increases in V_s between 2 hours' and 2 days' contact but after this no differences occur, equilibrium having been reached. The rise may be caused either by

further blocking of the resin pores by larger ions which have slowly entered the resin structure or by a slow change in the solution equilibrium producing smaller, highly charged ions. The state of the solution would probably be best indicated by resin uptakes at low contact times before the very slow rate of exchange mentioned in Section 2 has become important, and most of the results have been obtained with a contact time of 2 hours. Over this time interval the laws of resin diffusion mechanism are obeyed.

A few experiments were carried out with zirconium solution in perchloric and hydrochloric acids. Similarly shaped curves were obtained to those with nitric acid solutions, *i.e.*, a slow decrease in V_s with decreasing acidity and a rapid increase at acid concentrations less than 1N. With perchloric acid solutions the values of V_s were somewhat higher than with nitric acid

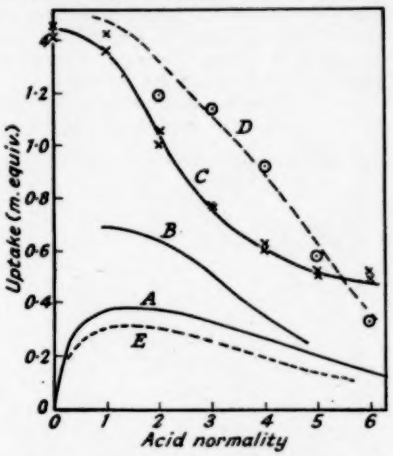


FIG. 11. *Comparison between zirconium and thorium uptake (m.-equiv.) from acid solution.*

A – Zr *from* HNO_3 (2 *hrs.' contact*).
B – Zr *from* HNO_3 (6 *days' contact*).
C – Th *from* HNO_3 (2 *hrs.' contact*).
D – Th *from* $HClO_4$ (2 *hrs.' contact*).
E – Zr *from* $HClO_4$ (2 *hrs.' contact*).

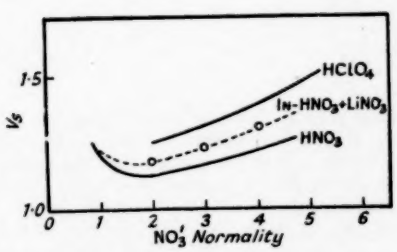


FIG. 12. *Determination of V_s for zirconium in nitric acid–lithium nitrate mixtures.*

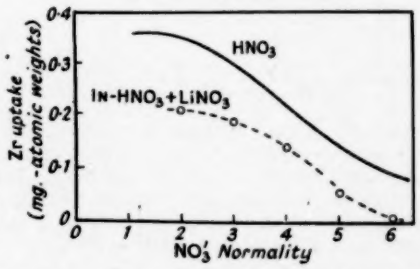


FIG. 13. *Uptake of zirconium from nitric acid–lithium nitrate mixtures.*

(see Fig. 8); insufficient experiments were carried out with hydrochloric acid to enable the exact path of the V_s curve to be determined.

As a comparison, runs were carried out with nitric and perchloric acid solutions of thorium in place of zirconium. The equivalent uptake after 2 hours was much greater than with the zirconium solutions (see Fig. 11) and the lowest value of V_s (with no added acid) was found to be 3·4. This emphasizes once again the great differences between the state of aqueous solutions of zirconium and of thorium salts.

To determine the effect on V_s of increasing the nitrate content of the solution without altering the acidity, a similar series of experiments was carried out using 1N-nitric acid and increasing the nitrate content by addition of lithium nitrate. The values of V_s, shown in Fig. 12, were slightly higher than when nitric acid only was used. Although this might mean an increase in the specific ionic charge of the zirconium species, it can equally well be explained by a small decrease in the hydrogen-ion concentration of the solution on addition of lithium nitrate; a slight shift in this direction will cause a considerable increase in the apparent value of V_s due to the formation of more polynuclear hydrolysis products, and approximate calculations show that

this effect will adequately explain the observed rise in V_s. The low zirconium uptake (Fig. 13) can be attributed to the formation of uncharged or anionic species, this being in agreement with the values for the $\overline{NO_3}/\overline{Zr}$ ratios observed in the work described in Section 3. It should be noted, however, that after a contact time of 1 day, the uptakes when using nitric acid only or nitric acid with lithium nitrate are very similar.

(7) pH *Measurements on Zirconyl Nitrate Solutions.*—pH Measurements have been made on solutions of zirconyl nitrate of different concentrations, a glass electrode being used in conjunction with a saturated calomel half-cell. Two methods were employed : (*a*) successive additions of zirconyl nitrate were made with mechanical stirring to 200 ml. of water and the pH was measured after 2 or 3 minutes; (*b*) a concentrated solution (1M, pH = 0) was diluted to give solutions of a number of different concentrations, and the pH measured over several days. The zirconyl nitrate concentration in each case varied between about 10^{-4} and 1M.

No measurements have been possible of the thermodynamic activities of the zirconium ions in solution and hence no satisfactory calculations can be made leading to the reaction mechanisms.

The results from the two methods are shown in Fig. 14. Curve *A* represents the best line through points obtained from six series of experiments using two different materials by method

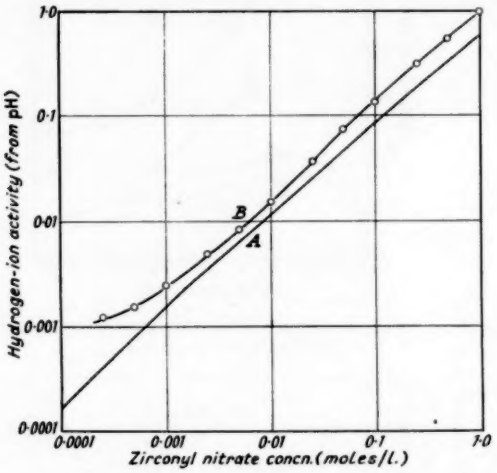


FIG. 14. *Relation between zirconium nitrate concentration and hydrogen-ion activity (from* pH *measurements).*

(*a*), and curve *B* shows the pH values found 10 days after dilution by method (*b*). It is seen that there are wide differences in the two curves over the whole concentration range, illustrating the slow attainment of equilibrium in the system. Indeed, it is not certain that the equilibria are completely reversible, since after 2—3 months' standing the corresponding curves still did not coincide. The obvious lack of equilibrium conditions in the solutions studied makes any calculations leading to the hydrolysis mechanism of little value, but further work on these lines might prove profitable.

DISCUSSION

The results obtained emphasize the complex nature of solutions of zirconium salts. Apart from the number of different species coexisting in solution, we have the additional complication of slow adjustment of equilibria; this difficulty may cause deviations in results observed with solutions prepared by somewhat different methods or even in the same solutions after different time intervals. As far as possible, similar methods of preparation have been employed for the solutions used, but small difference may easily enter in this way.

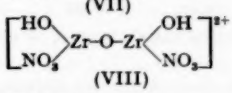
The evidence regarding ionic size obtained by measurements of resin diffusion coefficients and self-diffusion coefficients in solution confirms in a general way the results obtained by other workers, and it is abundantly clear that polynuclear-ion formation occurs even in solutions of quite high acidity. The resin diffusion method gives a semi-quantitative picture of the size of the ions, but satisfactory evidence is still lacking on the

mechanism of hydrolysis and polymerisation. The process of oxygen bridging is suggested as a probable mechanism, but the slow equilibrium changes, shown by the difference (and slow drift) in pH measurements when equilibrium is approached from the two sides, make any quantitative treatment rather suspect. Indeed, no direct evidence is yet forthcoming that the equilibria involved are truly reversible.

Nitric Acid Solution.—From the results on resin diffusion coefficients we can divide the system into three approximate acidity ranges. At acid concentrations less than 0·3N we have large polymerised species predominating, between 0·3 and 3N the species are approximately the size of the resin pores, and above 3N smaller ions which diffuse easily into the resin are most important. However, even these ions are larger than the cations from thorium nitrate solution which have been shown to be mainly of charge 4^+.

We can draw up a table (Table 3) which includes the most probable species, and proceed to eliminate certain of them by consideration of size, ionic charge, or nitrate content. For reasons of space, all possible species have not been included. Supposition of cationic species with a mean specific ionic charge greater than 2 or with a NO_3/Zr ratio greater than 2 is not necessary to explain the observations. If such species exist they are only present in very small amounts and have been omitted from the Table.

TABLE 3. *Possible zirconium species in nitric acid solution.**

Mean specific ionic charge:					
−2	0	0—1	+1	+2	NO_3/Zr
$[Zr(NO_3)_6]^{2-}$ (I)	—	—	—	—	6
$[Zr(OH)_2(NO_3)_4]^{2-}$ (II)	$[Zr(NO_3)_4]^0$ (II*a*)	—	—	—	4
—	$[Zr(OH)_2(NO_3)_2]^0$ (III)	—	$[Zr(OH)(NO_3)_2]^+$ (IV)	$[Zr(NO_3)_2]^{2+}$ (V)	2
—	$[(O{=}ZrNO_3)_2{=}O]^0$ (VI)	—	$[Zr(OH)_2(NO_3)]^+$ (VII)	$[Zr(OH)(NO_3)]^{2+}$ (IX)	1
			 (VIII)		
—	$[Zr(OH)_4]^0$ (X)	$[Zr_3O_5]^{2+}$ $[Zr_4O_7]^{2+}$, etc. (XIV)	$[Zr(OH)_3]^+$ (XI) $[(HO)_2Zr{-}O{-}Zr(OH)_2]^{2+}$ (XIII)	$[Zr(OH)_2]^{2+}$ (XII)	0

* For diagrammatic purposes simple formulæ have been incorporated in Table 3 (and in other places in the text). It would, however, be more correct to regard the species as being derived from the parent cation $[Zr(H_2O)_n]^{4+}$, where n may well be considered to be 6. Thus the relation between species (XII) and (XI) would be written as $[Zr(OH)_3(H_2O)_4]^{2+} \rightleftharpoons H^+ + [Zr(OH)_3(H_2O)_3]^+$ and so on. The reactions then fall into three types: (*a*) Competition of NO_3^- and OH^- with H_2O for positions in the co-ordination complex; (*b*) acid–base reactions often combined with (*a*); (*c*) condensation to form polynuclear cations with elimination of water.

The resin diffusion and self-diffusion data indicate, at low acid concentration, the existence of highly polymerised ions such as (XIV) in Table 3. With increasing acidity these will depolymerise to give the " dimer " (XIII), which may be one of the ions responsible for the " loop " in Fig. 3. The possible " depolymerisation " product $[Zr(OH)_3]^+$ is eliminated on account of its size, although at very much lower zirconium concentrations it may become important. The formation of $[Zr(OH)_2]^{2+}$ is not considered, since its specific charge of 2 is too high to agree with experimental data. From the dimer (XIII) we can proceed in a number of directions to (VII), (VIII), (IX), (V), or (IV). Species (VIII) can be eliminated on size considerations. Examination of the NO_3/Zr ratios found on a cation exchanger (see Section 3) gives us information on this point. Let us assume equilibria between species (XIII) and (VII):

$$[Zr_2O_3]^{2+} + 2H^+ + 2NO_3^- \overset{K_1}{\rightleftharpoons} 2[Zr(OH)_2(NO_3)]^+ + H_2O$$

Let us call $[Zr_2O_3]^{2+} = A$ and $[Zr(OH)_2(NO_3)]^+ = B$, and let X be the nitrate concentration. Then we have the relationships $K_1 = AX^4/B^2$ and $2A + B = Zr$ (Zr = total zirconium concentration). There also exist the cation-exchange equilibria :

$\frac{\bar{A}}{\bar{H}^2} = K_2 \cdot \frac{\bar{A}}{H^2}$; $\frac{\bar{B}}{\bar{H}} = K_3 \cdot \frac{B}{H}$ and $2\bar{A} + \bar{B} = \overline{Zr}$, where the bars represent the resin phase. From these relationships we arrive at an expression

$$k = \overline{Zr}f^2/(1 - f)X^4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $f = \bar{B}/\overline{Zr}$ and $k = K_3^2/2K_1K_2$. From this we obtain an equation for f:

$$\frac{f}{2} = \frac{X^2\sqrt{k/4\overline{Zr}}}{1 + X^2\sqrt{k/4\overline{Zr}}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

For a species containing one nitrato-group, the value of f is the value $\overline{X}/\overline{Zr}$ shown in Fig. 8. By substitution of experimental values at one value of X into equation (1) we can arrive at a value for k. Inserting this into equation (2) in conjunction with the value for $\overline{Zr}$ obtained from Fig. 9, we can see how the calculated values of f agree with the experimental $\overline{X}/\overline{Zr}$ curve (Table 4). Although the agreement is not very good, examination of the relations involved shows that the theoretical curves obtained by deriving similar equations from other possible reactions, *i.e.*, the formation of species (IX), (IV), or (V), do not agree nearly so well with the experimental curves.

TABLE 4.

X	$\overline{Zr}$	$\bar{B}/\overline{Zr}$ (calc.) * (*a*)	$\bar{B}/\overline{Zr}$ (calc.) * (*b*)	$\overline{X}/\overline{Zr}$ (exptl.)	X	$\overline{Zr}$	$\bar{B}/\overline{Zr}$ (calc.) * (*a*)	$\bar{B}/\overline{Zr}$ (calc.) * (*b*)	$\overline{X}/\overline{Zr}$ (exptl.)
1	7·0	0·01	0·02	0·05	4	3·0	0·28	0·33	0·28
2	6·3	0·06	0·07	0·09	5	2·0	0·48	0·56	0·56
3	5·0	0·14	0·16	0·16	6	1·3	0·72	0·83	0·98

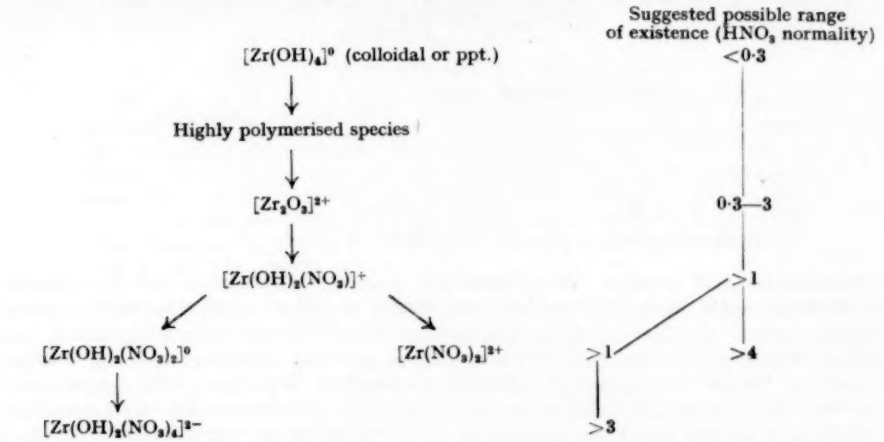
* (*a*) k found by matching at $X = 4$; (*b*) k found by matching at $X = 3$.

The above calculations make many approximations and neglect all activity coefficients. In addition, recognition is only made of the existence of two species, whereas the solution is almost certainly not so ideal. In the circumstances it is considered probable that the mononitrato-species is in fact $[Zr(OH)_2(NO_3)]^+$.

The experimental curve (Fig. 4) indicates that at acidities greater than about 4N a second species containing more nitrato-groups exists, and this, from considerations of ionic charge and size, is assumed to be $[Zr(NO_3)_2]^{2+}$. Electromigration studies and anion-exchange experiments show the presence of an anionic species at the higher acid concentrations. This may be $[Zr(OH)_2(NO_3)_4]^{2-}$ (II) or $Zr(NO_3)_6^{2-}$ (I) or possibly an intermediate uni-charged species. An uncharged species probably $[Zr(OH)_2(NO_3)_2]^0$, must be suspected and, although no direct proof is given, evidence for its presence is found in the experiments with mixed nitric acid–lithium nitrate solutions.

Nitric Acid and Lithium Nitrate Solutions.—The values obtained with mixed nitric acid–lithium nitrate solutions show that an increased nitrate concentration without increased acidity does not affect the nitrate content of the zirconium cationic species. We cannot therefore, under these conditions, suppose that a dinitrato-cationic complex makes any large contribution to the system. However, the initial cationic uptake on an exchange resin from the mixed nitric acid–lithium nitrate solutions is much smaller than for the corresponding pure nitric acid solutions and this, together with the facts that no significant differences in the zirconium uptake occur on an anionic resin and that there is little, if any, alteration in the value of the specific ionic charge, leads to the conclusion that an uncharged species is being formed under these conditions, probably $[Zr(OH)_2(NO_3)_2]^0$. It is probable that, by adjusting the nitrate–acidity conditions, a wide range of zirconium hydroxynitrato-complexes may be formed.

From these considerations, the following scheme is suggested :



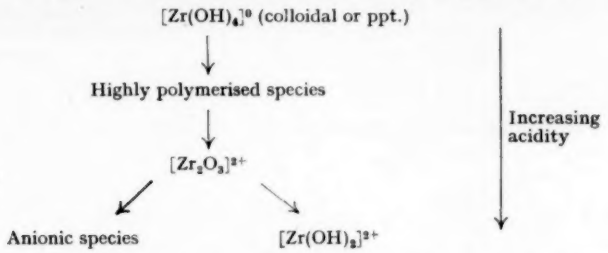
Perchloric Acid Solutions.—In perchloric acid solution we have very little, if any, complex cations formed by cation–anion interaction and, from an examination of the mean specific ionic charge curves, one must assume the formation in strongly acid solutions of the simple zirconyl radical $[Zr(OH)_2]^{2+}$. Connick and Reas (*loc. cit.*), by using extraction methods, have claimed that Zr^{4+} is the main monomeric zirconium species present in 1N- and 2N-perchloric acid solutions. The unlikely nature of this in solutions of the present concentrations seems to be confirmed by the fact that the uptake of zirconium from perchloric acid by a cation exchanger is rather slower than from nitric acid and very much slower than the uptake of thorium ion from nitrate solution. As with ion-exchange methods, the extraction technique (only Zr^{4+} ions will give an uncharged TTA complex soluble in the organic phase) favours the removal of more highly charged ions, and this tends to move the equilibria. This feature is, however, almost certainly more marked in extraction methods.

Electromigration and anion-exchange experiments show clearly the presence of zirconium in anionic complexes but the nature of these complexes is not clear. From this work, as well as from recent work by Sutton (*Nature*, 1952, **169**, 71) on the iron–perchlorate system, it is apparent that we must be much more careful before we assume that perchloric acid has no ability to form complexes. Indeed, some of the earlier work might well be reviewed in the light of this new information. It should, perhaps, be pointed out that Connick and his co-authors assume, but offer no experiments to prove, the absence of perchlorate complexing of zirconium.

The greater difficulty in removing zirconium from a cation-resin column with perchloric acid than with nitric acid (Lister, *J.*, 1951, 3123) may be explained by the small $[Zr(OH)_2]^{2+}$ ion being bound more tightly than the larger nitrato-ions found in nitric acid solution. In addition, the mean specific ionic charge of the zirconium species in perchloric acid solution is somewhat higher, but this fact alone is insufficient to explain the much higher degree of retention. Although a considerable proportion of zirconium may be present as anionic species, the introduction of the cation exchanger will cause a very large shift of the equilibria. A further explanation to correlate the difference in column behaviour of nitric and perchloric acids with the electromigration and anion-uptake data might be found in the relative amounts of anionic and uncharged species present in solution.

The greater ease of removal of zirconium from a column with sulphuric acid is easier to explain, since the cationic zirconium content of solutions in sulphuric acid is much smaller than in perchloric acid solution, and a smaller shift in the equilibrium would be expected to arise from the introduction of a cation-exchange resin. However, further experimental evidence on the position of the equilibria and the kinetics of all these systems is needed before a reliable explanation can be given.

We can then, for perchloric acid solutions of zirconium, suggest a scheme



Hydrochloric Acid Solution.—An examination of the results obtained with hydrochloric acid solutions again leads to the conclusion that a complex equilibrium system exists involving cationic, anionic, and uncharged species. The $\overline{X}$-$\overline{Zr}$ curves for hydrochloric acid solutions (Fig. 8) can be explained by the formation of a monochloro-complex and it is not necessary to assume the presence of any dichloro-complex. Electromigration experiments show very little movement of zirconium species in either direction, possibly indicating that an uncharged species is the predominating one. Anion-uptake experiments show that anions are present in solution, the equilibria involved moving to accommodate the removal of the small amount of anions originally taken up by the exchanger. The electromigration results may also be explained if similar amounts of cationic and anionic species are present with a very rapid adjustment of equilibria.

Similar conclusions as to the existence of cation–anion complexing have been arrived at by Adolf and Pauli (*Kolloid Z.*, 1921, **29**, 173) by measurements of conductance, pH, freezing points, and electromigration of $ZrOCl_2$ in solutions of different acid concentration. They have suggested complexes such as $[Zr(OH)_4,ZrO]^{2+}$, $[Zr(OH)_2Cl_4]^{2-}$, and $[Zr(OH)_4Cl_2]^{2-}$. The existence of the last ion has also been quoted by Blumenthal (*J. Chem. Educ.*, 1949, **26**, 472).

Sulphuric Acid Solution.—The existence of zirconium in complex anionic form in sulphuric acid solution was first demonstrated by Ruer (*loc. cit.*), and this has been amply confirmed by the present electromigration studies, by ion-exchange uptake experiments, and by column-elution behaviour (Lister, *loc. cit.*). We may again assume equilibria between cationic and anionic species, these equilibria lying far more to the anionic side than with any of the other acids studied. Electromigration and cation-exchange experiments have shown that in 1·5N-sulphuric acid solution the cationic species have disappeared completely and we are presumably left with equilibria between anionic and uncharged species. The presence of more than one anionic species has not been ruled out by these experiments.

We thank Dr. E. Glueckauf and Dr. J. S. Anderson for many helpful discussions, and the Director of the Atomic Energy Research Establishment for permission to publish this paper.

Atomic Energy Research Establishment,
Harwell, Didcot, Berks.

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828. *The Thermochemistry of Organo-arsenic Compounds. Part I. Cacodyl,* As_2Me_4.

By C. T. Mortimer and H. A. Skinner.

The heat of reaction of liquid cacodyl with iodine in methanol solution has been measured at 25° ($\Delta H_{corr.} = -19{\cdot}9 \pm 0{\cdot}2$ kcal. mole^{-1}), from which the relationship $\Delta Hf°(Me_2AsI, liq.) = \frac{1}{2}\Delta Hf°(Me_4As_2, liq.) - 9{\cdot}96$ kcal. is derived. From this a further relationship is got between the dissociation energy of the As–I bond in Me_2AsI (D_1), and the As–As bond in Me_4As_2 (D_2), *viz.*: $(D_1 - \frac{1}{2}D_2) = 29{\cdot}8 \pm 1{\cdot}5$ kcal. mole^{-1}. Some general considerations on the value of D_2 lead to the conclusion that D_1 probably lies within the range 47—50 kcal. mole^{-1}.

Tetramethyldiarsine (cacodyl) is highly reactive, spontaneously inflammable in air, and readily split at the As–As bond by halogens to give the secondary halides, Me_2AsX (see, *e.g.*, Sidgwick, "Chemical Elements and their Compounds," Oxford Univ. Press, 1950, p. 770). We have found that the reaction of cacodyl with iodine in methanol solution occurs rapidly at room temperature, and is suitable for thermochemical study. The heat of iodination represents, however, only a limited contribution to the thermochemistry of cacodyl and cacodyl iodide, giving merely the difference in heat content of the two substances. An attempt to supplement the information reported here by study of the controlled oxidation of cacodyl was not successful (owing to the complexity of the reaction), and the discussion of the present work is not as complete as we would otherwise have desired.

Experimental

Materials.—Cacodyl was prepared by Auger's method (*Compt. rend.*, 1906, **142**, 1153) by reducing cacodylic acid with hypophosphorous acid. The crude product was dried ($CaCl_2$) and distilled under a reduced pressure of nitrogen through a 6″ gauze-packed column. The fraction collected over the range 43·8—44·3°/11 mm. was redistilled *in vacuo* and sealed in thin weighed glass phials.

Cacodyl iodide was prepared from cacodylic acid by Burrows and Turner's method (*J.*, 1920, 1376) and purified by fractional distillation (b. p. 43·3—43·4°/10·5 mm.).

The methanol was a high-grade synthetic product, and the iodine was "AnalaR."

Calorimeter.—This was a narrow-necked 1-l. Dewar vessel, similar to that described by Charnley, Skinner, and Smith (*J.*, 1952, 2288), except that the tube-breaking platform and supports were of glass, and an inlet (for nitrogen) was let into the stopper in the neck of the Dewar flask. Temperature changes were recorded in terms of the resistance change of a thermistor element. The calorimeter was calibrated electrically by the substitution method.

Results

The iodination reaction was studied by breaking phials containing weighed amounts of cacodyl into a solution of iodine in methanol (750 c.c.) contained in the Dewar vessel. Normally, a small excess of iodine relative to cacodyl was used, but in some experiments this ratio was reversed. Preliminary experiments demonstrated the need to avoid the complications that might arise from oxidation of cacodyl. Accordingly, the air-space above the solution in the Dewar vessel was thoroughly swept out with nitrogen both before and during each experiment. Before the iodine solutions were made up, the methanol was alternately degassed and saturated with nitrogen until rid of all dissolved oxygen. These precautions proved to be sufficient, and we were able successfully with this technique to measure the negative heat of solution of cacodyl in methanol.

The observed heats of reaction (listed under $\Delta H_{obs.}$ in Table 1) refer to the equation:

$$Me_2As{\cdot}AsMe_2(liq.) + (n + 1)I_2(soln.) \longrightarrow \{2Me_2AsI + nI_2\}(soln.) \quad . \quad . \quad (1)$$

in which n is a small fraction, $< \pm 0{\cdot}1$. The values listed under $\Delta H_{corr.}$ refer to the heat of the idealized reaction,

$$Me_2As{\cdot}AsMe_2(liq.) + I_2(cryst.) \longrightarrow 2Me_2AsI(liq.) \quad . \quad . \quad . \quad . \quad (2)$$

and are derived from $\Delta H_{obs.}$ after correction for the various solution heats contained therein.

The heats of solution involved are:

(i) I_2(cryst.) in methanol, $\Delta H_{soln.} = 2{\cdot}07 \pm 0{\cdot}05$ kcal. mole^{-1} (Hartley and Skinner, *Trans. Faraday Soc.*, 1950, **46**, 621).
(ii) As_2Me_4(liq.) in methanol, $\Delta H_{soln.} = 0{\cdot}85 \pm 0{\cdot}04$ kcal. mole^{-1}.
(iii) Me_2AsI(liq.) in methanol, $\Delta H_{soln.} = 1{\cdot}08 \pm 0{\cdot}03$ kcal. mole^{-1}.
(iv) Me_2AsI(liq.) in methanol–I_2 solutions.

The correction term (iv) was the subject of a separate study, results of which are summarized in Table 2.

TABLE 1. *Iodination of cacodyl.*

Expt.	Cacodyl (g.)	I_2 (g.)	n (Eqn. 1)	m (Eqn. 4)	$\Delta H_{obs.}$ (kcal. mole^{-1})	$\Delta H_{corr.}$ (kcal. mole^{-1})
1	1·3826	1·8283	0·094	0·047	−21·43	−19·96
2	1·2830	1·7746	0·144	0·072	−22·16	−19·85
3	1·8134	2·5175	0·148	0·074	−22·33	−19·96
4	1·3785	1·9059	0·144	0·072	−22·32	−20·01
5	1·3509	1·4745	−0·097	—	−19·72	−19·81

Mean: $\Delta H_{corr.} = -19{\cdot}92$ kcal. mole^{-1}.
Final value: $\Delta H_{corr.} = -19{\cdot}9 \pm 0{\cdot}2$ kcal. mole^{-1}.

TABLE 2. *Solution of cacodyl iodide in methanolic iodine.*

Expt.	Me_2AsI (g.)	I_2 * (g.)	m (Eqn. 4)	$\Delta H_{obs.}$ (kcal. mole^{-1})
1	3·3206	0·0000	0	1·08
2	3·3371	0·2610	0·071	− 0·12
3	3·1619	0·8370	0·242	− 2·40
4	3·4963	1·7254	0·452	− 5·03
5	3·0454	2·5551	0·767	− 8·44
6	3·1185	3·55	1·04	−11·16

* Dissolved in 750 c.c. of methanol.

We have observed that the brown colour of dissolved iodine is almost instantaneously destroyed when equimolar proportions of cacodyl and iodine are mixed. But disappearance of the iodine colour occurs even when an *excess* (up to *ca.* 50%) of iodine is used. In accord with this, the addition of dimethyliodoarsine, Me_2AsI, to iodine solutions was found to destroy the brown colour (provided the former is in considerable excess). This "secondary" reaction is presumably the addition:

$$Me_2AsI + I_2 \rightleftharpoons Me_2AsI_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

in which the adduct may contain quinquevalent arsenic, or alternatively is the tri-iodide $Me_2As{\cdot}I\langle^{I}_{I}$.

To allow for the thermal effect of the secondary reaction in the experiments in which excess of iodine was used, a series of measurements on the heat of solution of iododimethylarsine in methanolic iodine was made. The values of $\Delta H_{obs.}$ in Table 2 refer to the reaction system:

$$Me_2AsI(liq.) + mI_2(soln.) \longrightarrow Products(soln.) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where the "products" may contain unchanged dimethyliodoarsine and iodine, as well as the tri-iodide Me_2AsI_3. It may be noted that the relationship between the factors m (in eqn. 4) and n (in eqn. 1) is simply $m = n/2$.

Discussion

The heat of reaction (2) relates the heats of formation of cacodyl and cacodyl iodide from elements in their standard states [whence $\Delta Hf°I_2$(cryst.) = 0] through the equation:

$$\Delta Hf°(Me_2AsI, liq.) = \tfrac{1}{2}\Delta Hf°(Me_4As_2, liq.) - 9{\cdot}96 \text{ kcal.} \quad . \quad . \quad (5)$$

This equation may be used as the starting-point in deriving the inter-relationship between the dissociation energies of the As–As bond in cacodyl, and the As–I bond in dimethyliodoarsine. Representing the dissociation processes by eqns. (6*a* and *b*),

$$Me_2AsI(g) \longrightarrow Me_2As(g) + I(g) - D_1 \text{ kcal.} \quad . \quad . \quad . \quad . \quad (6a)$$

$$Me_2As{\cdot}AsMe_2(g) \longrightarrow 2Me_2As(g) - D_2 \text{ kcal.} \quad . \quad . \quad . \quad (6b)$$

we obtain the appropriate thermochemical equation:

$$\Delta Hf°(Me_2AsI, g.) - \tfrac{1}{2}\Delta Hf°(As_2Me_4, g.) = \Delta Hf°(I, g.) - D_1 + D_2/2 \quad . \quad (7)$$

By use of the value $\Delta Hf°(\mathrm{I, g.}) = 25{\cdot}5$ kcal. mole^{-1} (*Nat. Bur. Standards*, Circular 500), and re-writing eqn. (5) in the form :

$$\Delta Hf°(\mathrm{Me_2AsI, g.}) - \tfrac{1}{2}\Delta Hf°(\mathrm{As_2Me_4, g.}) = \lambda_1 - \tfrac{1}{2}\lambda_2 - 9{\cdot}96 \quad . \quad . \quad (8)$$

where λ_1 and λ_2 are the latent heats of evaporation of dimethyliodoarsine and cacodyl respectively, the combination of eqns. (7) and (8) then gives :

$$(D_1 - \tfrac{1}{2}D_2) = 35{\cdot}4 + \tfrac{1}{2}\lambda_2 - \lambda_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Values of λ_2 and λ_1 are not available, but by combining the vapour pressure data here reported * with other data from the literature, we calculate the values $\lambda_1 = 10{\cdot}3$ and $\lambda_2 = 9{\cdot}4$ kcal. mole^{-1}. The error in these estimates may be as much as ± 1 kcal. These values reduce eqn. (9) to :

$$(D_1 - \tfrac{1}{2}D_2) = 29{\cdot}8 \pm 1{\cdot}5 \text{ kcal. mole}^{-1} \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The value of $(D_1 - \frac{1}{2}D_2)$ is appreciably larger than one would calculate from bond-energy values derived in the manner of Pauling (" Nature of the Chemical Bond," Cornell Univ. Press, New York, 1939, p. 53). Table 3 lists some mean bond energy terms ($\bar{D}$ values) of bonds to arsenic, based on thermal data taken mainly from the tables of selected values of chemical thermodynamic constants compiled by the National Bureau of Standards (Circular 500).

TABLE 3. *Mean bond energy terms of arsenic bonds.*

Molecule	$\Delta Hf°$(g.) (kcal. mole^{-1})	Bond	$\bar{D}$ (kcal.)	Molecule	$\Delta Hf°$(g.) (kcal. mole^{-1})	Bond	$\bar{D}$ (kcal.)
As	60·64	—	—	$AsBr_3$	− 32·0 *	As–Br	57·6
As_4	35·7	As–As	34·5	AsI_3	9·3 *	As–I	42·6
AsF_3	−218·3	As–F	111·9	As_4O_6	−283·4 *	As–O	73·3
$AsCl_3$	− 71·5	As–Cl	73·0	AsH_3	41	As–H	58·6

Values marked * are uncertain, owing to incomplete knowledge of the latent heats of sublimation. For $AsBr_3$ and AsI_3, the error in $\Delta Hf°$(g.) may be as much as ± 3 kcal. mole^{-1}, corresponding to an error of ± 1 kcal. in the derived $\bar{D}$ values.

The calculated difference (25·4 kcal.) between $\bar{D}$(As–I) and $\frac{1}{2}\bar{D}$(As–As)—from the values given in Table 3—is smaller by 4·4 kcal. than the experimental value $(D_1 - \frac{1}{2}D_2)$. The probable explanation is that the dissociation energy of the As–I bond in dimethyliodoarsine is larger than the mean As–I bond energy in arsenic tri-iodide, *i.e.*, $D_1 > \bar{D}$(As–I).

Earlier thermochemical studies on the alkylmercuric halides (Hartley, Pritchard, and Skinner, *Trans. Faraday Soc.*, 1950, **46**, 1019; Mortimer, Pritchard, and Skinner, *ibid.*, 1952, **48**, 220; Charnley and Skinner, *J.*, 1951, 1921) have shown that the redistribution reactions $HgR_2 + HgX_2 \longrightarrow 2RHgX$ are exothermic, from which it follows that the heat content of RHgX is larger than that calculated from the sum of the mean bond energy terms, $\bar{D}$(Hg–R) and $\bar{D}$(Hg–X), when these are derived individually from the compounds HgR_2 and HgX_2. The present results suggest that a similar exaltation in mean bond energy terms is present in the dimethylarsenic halides.

Whilst the analogy with the RHgX compounds provides a reasonable basis for assuming that $D_1 > \bar{D}$(As–I), it is useful to examine the equation we have derived, *i.e.* :

$$(D_1 - \tfrac{1}{2}D_2) = \bar{D}(\text{As–I}) - \tfrac{1}{2}\bar{D}(\text{As–As}) + 4{\cdot}4 \text{ kcal.} \quad . \quad . \quad . \quad (11)$$

according to the possibilities that D_2 is greater than, equal to, or less than $\bar{D}$(As–As). If $D_2 \geqslant \bar{D}$(As–As), then eqn. (11) requires that $D_1 > \bar{D}$(As–I), and that D_1 is at least 47 kcal. mole^{-1}. If the third possibility, $D_2 < \bar{D}$(As–As), were true, D_1 would remain greater than $\bar{D}$(As–I) unless D_2 were reduced by at least 8·8 kcal. relative to $\bar{D}$(As–As). Now in the As_4 molecule, the bond angles of 60° are generally considered to involve a considerable degree of strain, resulting in a weakening of the As–As bonds relative to the unstrained condition. In cacodyl, although its molecular configuration has not been

* An attempt to measure the vapour pressure of dimethyliodoarsine over a range of temperature in an apparatus similar to that described by Burg and Schlesinger (*J. Amer. Chem. Soc.*, 1937, **59**, 674) was not successful, owing to a slow but persistent attack on mercury.

determined, there is no necessity to assume strain, and from this viewpoint one might reasonably expect that here the As–As bond is stronger than in As_4. Pauling and Simonetta (*J. Chem. Phys.*, 1952, **20**, 801) have recently discussed the analogous P_4 molecule, in which they conclude there is a total strain energy of 22·8 kcal., or 3·8 kcal. per P–P bond. A similar strain energy in As_4 would raise the $\bar{D}$ value for a normal unstrained As–As bond from 34·5 kcal. in As_4 itself to 38·3 kcal. If we identify D_2 with the latter value, the value for D_1 becomes 49·0 kcal.

The general conclusion from these considerations is that the dissociation energy of the As–I bond in dimethyliodoarsine probably lies in the range 47—50 kcal. mole^{-1}, but a more exact assessment will be possible when information on the As–As bond dissociation energy in cacodyl becomes available. The direct determination of D_2 would be of value, not only in connection with the present work, but also as an indication of the strain energy in the As_4 molecule. The suggestion by Mashima (*ibid.*, p. 801) that the bonding in P_4 and As_4 involves *spd* trigonal pyramid bond orbitals contrasts with Pauling and Simonetta's views (*loc. cit.*), and a choice between these two viewpoints should be possible from a knowledge of D_2.

THE UNIVERSITY, MANCHESTER, 13. [*Received, July 17th*, 1952.]

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829. *Degradation of Quaternary Ammonium Salts. Part IX.* Attempts to Prepare Presumed Intermediates having Co-ordinately Linked Carbon.*

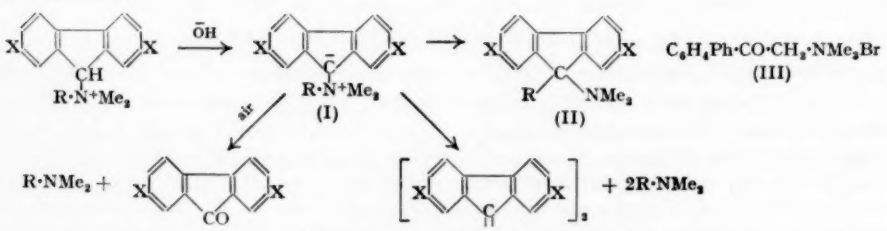
By W. R. BAMFORD, T. S. STEVENS, and J. W. WRIGHT.

Attempts are described to isolate compounds of the type (I), or to demonstrate their presence. The alkylation of fluorenylidenefluorenylamine, offering a route to (V), could not be effected. This base reacts with nitromethane, giving 9-nitromethylenefluorene. Related work on materials containing the *p*-phenylphenacyl radical is described.

IT is believed that the rearrangement,

$$Ph{\cdot}CO{\cdot}CH_2{\cdot}\overset{+}{N}Me_2{\cdot}CH_2Ph \xrightarrow{\text{Alkali}} Ph{\cdot}CO{\cdot}\bar{C}H{\cdot}\overset{+}{N}Me_2{\cdot}CH_2Ph \longrightarrow Ph{\cdot}CO{\cdot}CH(NMe_2){\cdot}CH_2Ph,$$

proceeds, as shown, by way of an intermediate zwitterion. When the corresponding rearrangement of benzylfluorenyldimethylammonium salts was observed (S. F. Marrian, Thesis, Glasgow, 1941) to give a red oil which soon lost its colour, changing into 9-benzyl-9-dimethylaminofluorene (II; R = CH_2Ph, X = H), it was natural to assume that the red oil was the unstable zwitterion (I) and to attempt the isolation of such materials in substance. During the progress of this work Wittig and Felletschin (*Annalen*, 1944, **555**, 133) solved the essential problem with the help of organo-lithium compounds as alkaline reagents, and we now present a summary of exploratory experiments and incidental observations.



As Ingold and Jessop (*J.*, 1929, 2357) could not isolate trimethylammonium 9-fluorenylide (I; R = Me, X = H), initial experiments were directed to the analogue (I;

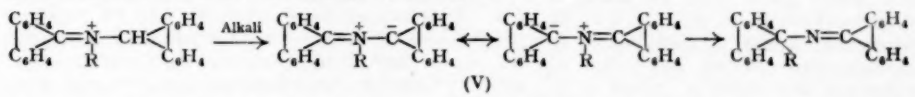
* Part VIII, *J.*, 1934, 279.

R = Me, X = Br) in the hope that it would be more stable and less soluble. Evaporation of a solution of 2 : 7-dibromofluorenyltrimethylammonium hydroxide gave a yellow precipitate which was easily oxidised in the air to dibromofluorenone and on attempted recrystallisation decomposed into trimethylamine and tetrabromodifluorenylidene. It was slightly soluble in water and on additon of hydrobromic acid yielded dibromofluorenyltrimethylammonium bromide. Attempts to combine the yellow compound with methyl iodide gave no decisive result.

Analogous experiments were carried out with trimethyl-*p*-phenylphenacylammonium bromide (III). The bromide gave with alkali a red product which could not be purified. Treatment of (III) with one equivalent each of methyl iodide and sodium methoxide, in the hope of converting any transient zwitterion into the salt $C_6H_4Ph{\cdot}CO{\cdot}CHMe{\cdot}NMe_3I$, yielded only the iodide corresponding to (III). Benzyldimethyl-*p*-phenylphenacylammonium bromide, when treated with alkali in presence or absence of methyl idoide, gave only the rearrangement product (IV) :

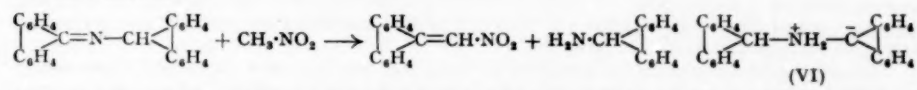
$$Ph{\cdot}C_6H_4{\cdot}CO{\cdot}CH_2{\cdot}\overset{+}{N}Me_2{\cdot}CH_2Ph\}Br^- \longrightarrow Ph{\cdot}C_6H_4{\cdot}CO{\cdot}CH(CH_2Ph){\cdot}NMe_2 \qquad \text{(IV)}$$

It was thought that in a system offering an alternative site for the anionic charge, the postulated intermediate, for example (V), might be more stable :



(V)

This type of structure is the equivalent of that assigned by Staudinger to his nitrenes, which Taylor, Owen, and Whittaker (*J.*, 1938, 206) regard as ethyleneimine derivatives; here the peculiar character of the fluorene system would favour the linear zwitterionic structure. Numerous attempts to prepare quaternary salts of fluorenylidenefluorenylamine by combination with allyl and other alkyl halides and toluenesulphonates failed, and model experiments on the addition of alkyl halides and esters to benzylidenefluorenylamine and fluorenone methylimine were also unsuccessful. Fluorenylidenefluorenylamine, best prepared from 9 : 9-dialkoxyfluorene and fluorenylamine, was also formed when benzylidenefluorenylamine was treated with excess of fluorenylamine. The use of nitromethane as a solvent in experiments with fluorenylidenefluorenylamine led to the production of 9-nitromethylenefluorene, which could not be obtained directly from fluorenone and nitromethane :



(VI)

The *addition* of nitromethane to simpler azomethines is recorded (*e.g.*, Leonard, Leubner, and Burke, *J. Org. Chem.*, 1950, **15**, 979), giving products which yield alkylidenenitromethanes on treatment with acid.

In attempts to prepare the Schiff bases $[\cdot C_6H_4]_2 > CH{\cdot}N{:}CH{\cdot}CO{\cdot}Ph$ and $Ph{\cdot}CO{\cdot}CH_2{\cdot}N{:}CH{\cdot}COPh$ from phenylglyoxal and the appropriate amines, the only products obtainable were fluorenylidenefluorenylamine and 2 : 5-diphenylpyrazine respectively.

Pinck and Hilbert (*J. Amer. Chem. Soc.*, 1946, **68**, 2013), observing that difluorenylamine dissolves in liquid ammonia or in alcoholic alkali to deep-blue solutions, attributed the colour to the zwitterion (VI). We have observed a similar colour with fluorenylidenefluorenylamine, less intense colours with difluorenylalkylamines, and none with simple aminofluorenes or fluorenone imines. Benzylideneaminofluorene gives a red colour. A satisfactory interpretation of these colours is lacking.

Experimental

2 : 7 : 9-*Tribromofluorene*.—Bromine (2 mols.), added to 9-bromofluorene (1 mol.) in warm chloroform, caused a vigorous reaction, and the *product* crystallised from chloroform in colourless needles, m. p. 196—197° (Found : C, 38·7; H, 2·0; Br, 59·9. $C_{13}H_7Br_3$ requires C, 38·7;

H, 1·8; Br, 59·5%). By oxidation with potassium dichromate and sulphuric acid in acetic acid it gave 2 : 7-dibromofluorenone (mixed m. p.). Heated at 100° for 6 hours in chlorobenzene with a slight excess of trimethylamine, the tribromofluorene gave 2 : 7-*dibromo*-9-*fluorenyltrimethylammonium bromide* as a precipitate which crystallised from water in prisms, m. p. 210° (decomp.) (Found : C, 41·4; H, 3·7; N, 3·2; Br, 52·4. $C_{16}H_{16}NBr_3$ requires C, 41·6; H, 3·5; N, 3·0; Br, 51·9%) or in hydrated needles (Found : C, 39·5; H, 3·8; Br, 50·1. $C_{16}H_{16}NBr_3,H_2O$ requires C, 40·0; H, 3·8; Br, 50·0%).

Addition of caustic alkali to an aqueous solution of the quaternary bromide gave a yellow precipitate; this could not be freed from bromide ion by filtration and washing, and when dissolved in benzene or carbon tetrachloride quickly decomposed with formation of a high-melting red solid, presumably tetrabromodifluorenylidene. A solution of the bromide was treated with one equivalent of silver sulphate until free from bromide and silver ions, and the sulphate precipitated by an exact equivalent of barium hydroxide. The filtered solution was evaporated in a desiccator over sodium hydroxide, giving a white precipitate which became yellow. This again could not be purified; it was slightly soluble in water and was reconverted into the quaternary bromide on treatment with hydrobromic acid. Attempts to combine it with methyl iodide gave no decisive result. For comparison, the synthesis of the expected product, 2 : 7-dibromo-9-methyl-9-fluorenyltrimethylammonium iodide, was undertaken as follows. By treating 2 : 7-dibromo-9-methylfluoren-9-ol with hydrogen bromide, after Sieglitz and Jassoy (*Ber.*, 1922, **55**, 2032), 2 : 7 : 9-*tribromo*-9-*methylfluorene*, m. p. 190—191°, was obtained (Found : C, 40·5; H, 2·3; Br, 57·4. $C_{14}H_9Br_3$ requires C, 40·3; H, 2·1; Br, 57·5%). When heated with trimethylamine in chlorobenzene at 100° for 4 hours, it gave brownish crystals which formed pale-yellow needles, m. p. 205°, from benzene. This nitrogen-free compound was identical (mixed m. p.) with 2 : 7-dibromo-9-methylenefluorene (Sieglitz and Jassoy, *loc. cit.*).

2 : 7-*Dibromo*-9-*dimethylaminofluorene* was prepared by heating tribromofluorene with dimethylamine in benzene at 70—80° for 3 hours. Isolated *via* the sparingly soluble hydrochloride, the base crystallised from aqueous alcohol in needles, m. p. 80° (Found : N, 4·1. $C_{15}H_{13}NBr_2$ requires N, 3·8%). The *picrate* formed yellow leaflets (from acetic acid), m. p. 225—230° (decomp.) (Found : N, 9·6. $C_{15}H_{13}NBr_2,C_6H_3O_7N_3$ requires N, 9·4%).

Trimethyl-p-*phenylphenacylammonium Bromide.*—*p*-Phenylphenacyl bromide (Carpenter and Turner, *J.*, 1934, 870) combined with trimethylamine in cold benzene; the quaternary bromide, recrystallised from methanol, melted at 230° (decomp.) (Found : C, 61·4; H, 5·8; N, 4·2; Br, 23·8. $C_{17}H_{20}ONBr$ requires C, 61·1; H, 6·0; N, 4·2; Br, 23·9%); the related *picrate*, prepared in methanol, melted at 178° (Found : C, 57·4; H, 4·5; N, 11·5. $C_{17}H_{20}ON,C_6H_2O_7N_3$ requires C, 57·3; H, 4·6; N, 11·6%). A solution of the bromide in a slight excess of 2N-sodium hydroxide became red on being warmed; the mixture was allowed to evaporate on a steam-bath; a smell of trimethylamine became evident, and the dark-red residue, washed free from bromide ion with hot water, contained no nitrogen and melted at 142°. It became discoloured in daylight.

Trimethyl-*p*-phenylphenacylammonium bromide was heated under reflux in a slight excess of methyl-alcoholic sodium methoxide with methyl iodide for several hours. Ether then precipitated from the cooled solution crude trimethyl-*p*-phenylphenacylammonium iodide, which yielded the picrate, m. p. and mixed m. p. 178°. The last m. p. was depressed on admixture with trimethyl-α-methyl-*p*-phenylphenacylammonium picrate prepared as follows. Crystallised from benzene and from alcohol, 4-propionyldiphenyl melted at 96—97°; Long and Henze (*J. Amer. Chem. Soc.*, 1941, **63**, 1939) give 89°; Campbell and Chattaway (*Proc. Roy. Soc.*, 1942, *B*, **130**, 440) give 98°. Bromination in acetic acid at 50° gave the α-bromo-derivative, plates (from alcohol), m. p. 102—103° (Found : C, 61·7; H, 4·4; Br, 27·6. Calc. for $C_{15}H_{13}OBr$: C, 62·3; H, 4·5; Br, 27·7%). The same product was obtained by heating propionyldiphenyl with *N*-bromosuccinimide in a bath at 130° for several hours; it was extracted with carbon tetrachloride and crystallised from alcohol. The m. p. 79—80° is recorded by Collet (*Compt. rend.*, 1897, **125**, 306). The bromo-ketone was heated for an hour at 100° with trimethylamine in benzene; the resulting quaternary bromide crystallised from methanol–ether in needles, m. p. 218° (decomp.), and the derived *picrate*, prepared in methanol, had m. p. 186° (Found : C, 58·2; H, 4·9; N, 11·2. $C_{18}H_{22}ON,C_6H_2O_7N_3$ requires C, 58·1; H, 4·9; N, 11·3%).

Benzyldimethyl-p-*phenylphenacylammonium bromide* was rapidly formed from phenylphenacyl bromide and benzyldimethylamine in warm benzene. Crystallised from methanol–ether, it melted at 207° (decomp.) (Found : C, 67·5; H, 5·7; Br, 19·4. $C_{23}H_{24}ONBr$ requires C, 67·3; H, 5·9; Br, 19·5%). Addition of sodium hydroxide to the hot aqueous solution of the

bromide caused rapid separation of a yellow oil, *ω-benzyl-ω-dimethylamino*-p-*phenylacetophenone*, which solidified on cooling and formed yellow crystals (from methanol), m. p. 103—104° (Found : C, 83·9; H, 6·8; N, 4·2. $C_{23}H_{23}ON$ requires C, 83·9; H, 7·0; N, 4·3%). The *methiodide*, prepared in hot methanol, crystallised from methanol–ether in pale yellow flakes, m. p. 194° (Found : C, 61·1; H, 5·4; I, 26·9. $C_{24}H_{26}ONI$ requires C, 61·2; H, 5·5; I, 27·0%). When the quaternary bromide was heated in methanol with sodium hydroxide or methoxide and methyl iodide, it gave only the methiodide of the rearranged product, m. p. 190°.

Fluorenylidenefluorenylamine.—In our hands the method of Ingold and Wilson (*J.*, 1933, 1499) gave yields of only 7%. Slightly better results were obtained by refluxing equimolecular quantities of sodium ethoxide, fluorenylamine hydrochloride, and fluorenone in anhydrous alcohol for 6—7 hours. The deep green colour of the filtered solution faded on cooling, and pale yellow fluorenylidenefluorenylamine separated on cooling. Alternatively fluorenylamine hydrochloride (5 g.) was treated with excess of alkali, and the base dissolved in toluene (70 c.c.). To the toluene solution 9 : 9-dimethoxyfluorene (Schlenk and Bergmann, *Annalen*, 1929, **463**, 199) (5·2 g.) was added and the whole refluxed for several hours. The oily residue from the evaporation of the toluene, taken up in alcohol, afforded crystals of fluorenylidenefluorenylamine (1·7 g.).

The Schiff base did not combine with methyl iodide or sulphate in boiling benzene. Boiled for some hours with methyl sulphate in nitromethane it gave, on concentration after filtration, dark brown crystals of *9-nitromethylenefluorene* which crystallised from benzene in brown needles, m. p. 133—134° (Found : C, 75·9; H, 4·1; N, 5·9. $C_{14}H_9O_2N$ requires C, 75·3; H, 4·0; N, 6·3%). The same substance was produced by heating the base in nitromethane alone; but not from fluorenone and nitromethane, alone or in presence of sodium methoxide or zinc chloride. Prolonged refluxing of fluorenylidenefluorenylamine with allyl iodide, alone or in xylene, gave small quantities of brown solid which could not be purified.

Allyl toluene-*p*-sulphonate (Gilman and Beaber, *J. Amer. Chem. Soc.*, 1925, **47**, 522) distilled at 135—140°/0·5—1·0 mm. without explosion or conspicuous decomposition. The ester (0·6 g.) was refluxed for 5 hours with the Schiff base (0·5 g.) in dry toluene (25 c.c.) with exclusion of moisture. Orange crystals separated which melted at 240° (decomp.). They were identified as *9-iminofluorene toluene*-p-*sulphonate* by analysis (Found : C, 68·0; H, 4·8; S, 9·0. $C_{13}H_9N,C_7H_8O_3S$ requires C, 68·4; H, 4·8; S, 9·1%) and by mixed m. p. of iminofluorene, liberated by sodium hydroxide and crystallised from ligroin. The same product was obtained when the base and ester were heated alone at 100°.

Benzaldehyde and fluorenylamine afforded (Schmidt, *Ber.*, 1908, **41**, 1243) benzylideneaminofluorene (71%) with some fluorenylideneaminofluorene. The latter azomethine is produced in quantity when the former is heated under reflux with excess of aminofluorene in alcohol for several hours. A solution of benzylideneaminofluorene (2 g.) in freshly distilled methyl iodide (4 c.c.) was kept in the dark for several months. The resulting solid was resolved into fractions, m. p. 240—241° (decomp.) and 177° (decomp.), by crystallisation from chloroform–ligroin. The latter, very pale yellow needles, appeared to be *fluorenylmethylamine hydriodide* (Found : C, 52·4; H, 4·3; I, 39·1. $C_{14}H_{14}NI$ requires C, 52·1; H, 4·4; I, 39·3%); the corresponding *picrate*, yellow needles from alcohol, melted at 210° (decomp.) (Found : N, 13·4. $C_{14}H_{13}N,C_6H_3O_7N_3$ requires N, 13·2%). The higher-melting fraction, of variable composition, gave an evanescent blue colour when boiled in alcoholic sodium ethoxide solution; and the basic product of this reaction yielded the picrate, m. p. 210° (decomp.). The same picrate was isolated when the azomethine and methyl sulphate were refluxed in dry ethyl acetate.

9-Methyliminofluorene was prepared by Reddelien's method (*Ber.*, 1921, **54**, 3130) which also afforded much difluorenyl and difluorenylidene. It did not combine with 9-bromofluorene or with phenacyl bromide on long boiling in toluene or under other conditions.

In an attempt to prepare 9-fluorenyl toluene-*p*-sulphonate, fluoren-9-ol (1·8 g.) was fused with toluene-*p*-sulphonyl chloride (2·5 g.) and the finely ground mass shaken for several hours with 5% potassium hydroxide solution. The only isolable product was difluorenyl ether, m. p. 228° (Found : C, 89·8; H, 5·2. Calc. for $C_{26}H_{18}O$: C, 90·1; H, 5·2%). Diazofluorene (2 g.) and toluene-*p*-sulphonic acid (6 g.; dried at 120°) were allowed to react in benzene solution. The washed and dried liquid gave on evaporation a solid evidently containing difluorenylidene. Crystallised from amyl alcohol, this yielded difluorenyl, m. p. and mixed m. p. 245° (Found : C, 94·8; H, 5·4. Calc. for $C_{26}H_{18}$: C, 94·6; H, 5·4%).

Freshly distilled phenylglyoxal (Riley and Gray, *Org. Synth.*, 1935, **15**, 67) was heated under reflux with pure fluorenylamine in alcohol for 30 minutes. The resulting solid crystallised from alcohol in fine yellow needles, identical (mixed m. p.) with fluorenylidenefluorenylamine (Found :

C, 90·8; H, 5·0. Calc. for $C_{26}H_{17}N$: C, 90·9; H, 5·0%). Phenylglyoxal (3·2 g.), ω-aminoacetophenone hydrochloride (3·5 g.), and sodium carbonate (2 g.) were heated on the water-bath for 30 minutes. Alcohol then extracted from the mixture 2 : 5-diphenylpyrazine, m. p. 195°, and no phenacylideneacetophenone could be isolated. Phenylglyoxal did not react with aminoacetophenone hydrochloride in boiling alcohol.

Colour Reactions of Fluorenylamine Derivatives.—A solution of difluorenylamine (0·15 g.) in liquid ammonia (6 c.c.) was deep blue and remained so for over 2 years (cf. Pinck and Hilbert, *loc. cit.*). *Difluorenylmethylamine* gave similarly a pale blue-green colour in liquid ammonia and a blue colour in alcoholic sodium ethoxide. This base was obtained from difluorenylamine (m. p. 201°; 0·4 g.) which was kept for 8 hours with formic acid (1·4 c.c.) and 35% formaldehyde solution (0·9 c.c.) and then heated on the water-bath for 4 hours. Concentrated hydrochloric acid was added in slight excess, the solution evaporated to dryness, and the free base (0·35 g.) liberated and crystallised from benzene–ligroin. It formed large prisms, m. p. 153° (Found: C, 90·2; H, 6·0. $C_{27}H_{21}N$ requires C, 90·3; H, 5·9%). *Allyldifluorenylamine* dissolved in alcoholic sodium ethoxide solution containing a little acetone with a blue-green colour which persisted for several hours. It was prepared by refluxing 9-bromofluorene (1·2 g.) and allylamine (0·6 c.c.) in acetonitrile (3 c.c.) for 30 minutes. The solid hydrobromide gave on basification allyldifluorenylamine, prisms, m. p. 195°, from benzene–ligroin (Found: C, 90·7; H, 5·9. $C_{29}H_{23}N$ requires C, 90·4; H, 5·9%). Fluorenylidenefluorenylamine gave an intense blue colour in warm alcoholic sodium ethoxide, and benzylidenefluorenylamine a red colour. No colours were given by 9-anilino-, 9-methylimino-, or 9-phenylimino-fluorene.

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830. *Amides of Vegetable Origin. Part II.* Stereoisomeric* N-iso-*Butylnona*-1 : 5-*diene*-1-*carboxyamides and the Structure of Pellitorine.*

By L. CROMBIE.

Syntheses of the *trans*-1 : *trans*-5-, *trans*-1 : *cis*-5-, and *cis*-1 : *trans*-5-stereoisomers of *N-iso*butylnona-1 : 5-diene-1-carboxyamide have been effected. The *trans*-1 : *trans*-5-compound is identical with a previously described isomer of, unproven configuration. Since the *cis*-1 : *cis*-5-compound is already known the four possible geometrical isomers are now available as in the *N-iso*butylundeca-1 : 7-diene-1-carboxyamide series. The configurations, assigned on a basis of reaction stereospecificity, are supported by spectroscopic investigation.

All of the compounds are poor sialogogues and have low insecticidal potencies. None is identical with natural pellitorine and the currently accepted structure, like that of herculin (Part I), is incorrect. Nevertheless, in contrast with herculin, it has been possible to re-isolate pellitorine and establish its identity with the material described by Jacobson (*J. Amer. Chem. Soc.*, 1949, **71**, 366).

THE roots of *Anacyclus pyrethrum* D.C. (known in the older literature as *Anthemis pyrethrum*, Spanish chamomile, or pellitory of Spain) contain a sialogogue and stomachic principle which has been used in medicine for many centuries. When chewed, the effect is not immediate though the onset of a characteristic burning taste is rapid. It has been recommended for the alleviation of toothache and bronchitis and was prescribed by Arabian physicians for rigors. The compound responsible aroused the interest of various investigators (*inter al.*, Bucheim, *Arch. Exp. Path. Pharm.*, 1876, **5**, 455; Dunstan, *J.*, 1895, **67**, 100; Schneegans, *Pharm. Ztg.*, 1896, **41**, 669) and was isolated as a crystalline solid by Gulland and Hopton (*J.*, 1930, 6) who demonstrated that it was a diene which on

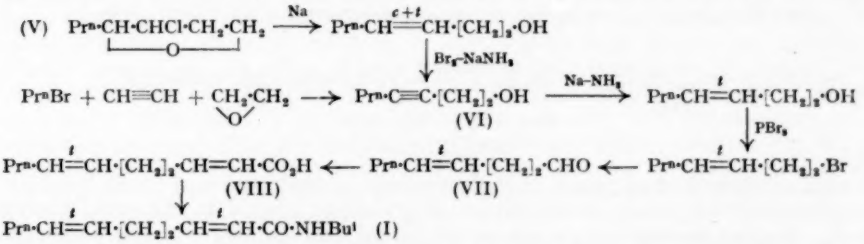
* Part I, *J.*, 1952, 2997.

hydrogenation yielded *N-iso*butylnonane-1-carboxyamide. As a result of degradative experiments with permanganate, Jacobson (*J. Amer. Chem. Soc.*, 1949, **71**, 366) assigned the unsaturation to the 1 : 5-positions, though no comment was made on the stereochemistry. Like a number of other sialogogue *iso*butylamides it is insecticidally active (Jacobson, *loc. cit.*; Crombie, Part I, *loc. cit.*).

The investigation recorded here was concurrent with that described in Part I and had similar objectives, *viz.*, the syntheses of the four possible geometrical isomers (I—IV). During its progress, preparations of the *cis*-1 : *cis*-5-stereoisomer (IV) (Raphael and Sondheimer, *J.*, 1950, 120) and a second compound of then uncertain configuration (Jacobson, Abstr. Papers presented at the 116th Meeting Amer. Chem. Soc., 1949; *J. Amer. Chem. Soc.*, 1950, **72**, 1489) were reported. Syntheses of the *trans*-1 : *trans*-5- (I), the *cis*-1 : *trans*-5- (II), and the *trans*-1 : *cis*-5-compound (III) are described below.

trans- and *cis*-Hept-3-enol were needed for the preparation of (I) and (III). A hept-3-enol is readily available from the mixed *cis*- and *trans*-3-chloro-2-*n*-propyltetrahydrofuran (V) (Normant, *Compt. rend.*, 1948, **226**, 773) by treatment with sodium but infra-red evidence and the melting point of its *p*-diphenylylurethane indicate that it is a mixture of *cis*- and *trans*-forms (cf. Crombie and Harper, *J.*, 1950, 1714). It must therefore first be converted into hept-3-ynol (VI), by bromination and dehydrobromination with sodamide in liquid ammonia. The latter alcohol was also made by a direct synthesis from acetylene (cf. Zoss and Hennion, *J. Amer. Chem. Soc.*, 1941, **63**, 1151; Sondheimer, *J.*, 1950, 877; Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1292), the pentyne not being isolated but converted directly into heptynol by addition of a further mol. of sodamide and excess of ethylene oxide. Besides the hept-3-ynol (3 : 5-dinitrobenzoate, m. p. 62°) there was isolated a higher-boiling acetylenic alcohol (3 : 5-dinitrobenzoate, m. p. 62°, but depressed on admixture with the former). Analysis of derivatives, microhydrogenation, and infra-red evidence show it to be the monohept-3-ynyl ether of ethylene glycol formed by reaction of hept-3-ynol with another mol. of ethylene oxide (cf. Leese and Raphael, *J.*, 1950, 2725).

Reduction of hept-3-ynol with sodium in liquid ammonia—a stereospecific process (Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 216, 2683)—gave *trans*-hept-3-enol (*p*-diphenylurethane, m. p. 105°) which was converted successively into the bromide, the Grignard reagent, and, by treatment with ethyl orthoformate, *trans*-oct-4-enal (VII) (2 : 4-dinitrophenylhydrazone, m. p. 110°). The Doebner reaction yielded nona-*trans*-1 : *trans*-5-diene-1-carboxylic acid (VIII), m. p. 43° [characterised like all other acids



described here as the *p*-bromophenacyl ester (see Table)]. This crystallinity is taken as evidence of its freedom from the small quantities of β-unsaturated acid sometimes encountered in such preparations and from other stereoisomers. Treatment with thionyl chloride and then *iso*butylamine produced the required *N-iso*butylnona-*trans*-1 : *trans*-5-diene-1-carboxyamide (I).

The amide (I) was identical (mixed m. p.) with the *iso*butylamide prepared by Jacobson (*loc. cit.*). Such a conclusion is to be expected as the oct-4-enal which he used was derived from oct-4-enol, in turn obtained from the ring fission of a mixture of *cis*- and *trans*-3-chlorotetrahydro-2-*n*-propylpyran with sodium. This reaction was subsequently shown (in the pyran series) to yield a *trans*-alcohol (Crombie and Harper, *J.*, 1950, 1707; *Nature*, 1949, **164**, 1053). Jacobson's yield at the Doebner stage was improved from 17% to 48%

by using a lower temperature and a longer reaction time (Boxer and Linstead, *J.*, 1931, 740) and the m. p. of this *trans-trans*-acid was 8° higher than his.

A convenient intermediate for the preparation of *N-iso*butylnona-*cis*-1 : *trans*-5-diene-1-carboxyamide is *trans*-non-5-en-1-yne (IX). The type of preparation used for its homologue, *trans*-undec-7-en-1-yne, in Part I, is here contra-indicated as sodium acetylide causes dehydrohalogenation of the hept-3-enyl halide to hepta-1 : 3-diene (Raphael and Sondheimer, *loc. cit.*). A coupling reaction between propargylmagnesium bromide and *trans*-hex-3-enyl bromide was therefore investigated. It is known (Young, Roberts, and Wax, *J. Amer. Chem. Soc.*, 1945, **67**, 841) that allylmagnesium halide gives almost entirely normal-chain diene hydrocarbon when allowed to react with but-2-enyl chloride, and even with pure 1-methylallyl chloride only 24% of branched-chain material is formed. The *trans*-hex-3-enyl bromide used in this work was prepared from 1-vinylbutyl carbinol by reaction with phosphorus tribromide and is therefore mainly primary (cf. Bouis, *Ann. Chim.*, 1928, **9**, 403; Winstein and Young, *J. Amer. Chem. Soc.*, 1936, **58**, 104). It was hoped that the coupling product would be essentially straight chain in this case too. The allylic bromide reacted vigorously with propargylmagnesium bromide (Prévost, Gaudemar, and Honigberg, *Compt. rend.*, 1950, **230**, 1186), yielding a product (b. p. 136—144°) still containing a considerable quantity of bromine. Infra-red examination confirmed the presence of C≡CH and *trans*-CH_2·CH=CH·CH_2 groupings,* so the product was treated with an excess of ethylmagnesium bromide and carboxylated. The required *trans*-non-5-en-1-yne-1-carboxylic acid (X) was readily isolated from the product and purified by distillation (overall yield 25%). Its structure was confirmed by hydrogenation to nonane-1-carboxylic acid and by its infra-red spectrum : contamination with the branched-chain isomer (XI) was negligible [C≡C·CO_2H 2230 cm.$^{-1}$ (strong); C—H bending indicating internal *trans*-double bond 969 cm.$^{-1}$ (medium); absorption at 995 cm.$^{-1}$, indicating CH_2=CH, very weak; the other vinyl absorption region at 910 cm.$^{-1}$ could not be used decisively in the liquid film because of absorption here by the dimeric carboxylic acid grouping].

The coupling of a Grignard reagent from *trans*-hex-3-enyl bromide with propargyl bromide was avoided, as crotylmagnesium bromide and allyl bromide (Young, Roberts, and Wax, *loc. cit.*) yield a mixture of normal and branched-chain materials. Also much allene formation might be expected (Prévost *et al.*, *loc. cit.*). The components of the crude coupling product have not been further examined and no marked improvement of yield was noted by the addition of cuprous chloride catalyst.

$$Pr^n\cdot CH{=}CH\cdot CH_2Br + Br\cdot Mg\cdot CH_2\cdot C{\equiv}CH \longrightarrow Pr^n\cdot CH{=}CH\cdot[CH_2]_2\cdot C{\equiv}CH \quad (IX)$$

$$\downarrow$$

$$Pr^n\cdot CH{=}CH\cdot[CH_2]_2\cdot CH{=}CH\cdot CO\cdot NHBu^t \xleftarrow{\text{3 stages}} Pr^n\cdot CH{=}CH\cdot[CH_2]_2\cdot C{\equiv}C\cdot CO_2H$$

(II) (X)

$$Pr^n\cdot CH(CH_2\cdot C{\equiv}C\cdot CO_2H)\cdot CH{=}CH_2 \quad (XI)$$

Partial catalytic hydrogenation of the enyne acid yielded nona-*cis*-1 : *trans*-5-diene-1-carboxylic acid which was converted into its *iso*butylamide, a liquid, by the oxalyl chloride method. Another specimen was made by the partial hydrogenation of *trans-N-iso*butylnon-5-en-1-yne-1-carboxyamide.

The reaction sequence for the preparation of *N-iso*butylnona-*trans*-1 : *cis*-5-diene-1-carboxyamide was similar to that for the *trans*-1 : *trans*-5-isomer except that the hept-3-ynol was converted into *cis*-hept-3-enol (*p*-diphenylylurethane, m. p. 85°). The intermediate *cis*-oct-4-enal was characterised as its 2 : 4-dinitrophenylhydrazone (m. p. 81°). A preliminary note on this synthesis has already been published (Crombie and Harper, *Nature*, *loc. cit.*). Data are given in the Table. A discussion of the stereospecificity of catalytic semihydrogenation is given elsewhere (Part I; Crombie, *Quart. Reviews*, 1952, **6**, 101), and the purity of the isomers made by this procedure is subject to the reservations mentioned there. The *cis-cis*-isomer was prepared by semihydrogenation of *N-iso*butyl-

* No absorption at *ca.* 1950 cm.$^{-1}$ was detected, indicating the absence of allenic material.

nona-1 : 5-diyne-1-carboxyamide by Raphael and Sondheimer (*loc. cit.*) who kindly made a specimen available for spectroscopic measurements.

Some support for the configurations assigned by the mode of synthesis comes from the order of melting points of the *p*-bromophenacyl esters of the three 1 : 5-diene-acids. These decrease (*trans*-1 : *trans*-5 > *cis*-1 : *trans*-5 > *trans*-1 : *cis*-5) as chain bending increases.

Nonadiene-1-carboxylic acids and iso*butylamides.*

			p-Bromophenacyl ester	*iso*Butylamide				
	B. p./mm.	n_D^{20} *	M. p.	B. p./mm.	n_D^{20} *	No. of C : C †	$\lambda_{max.}$ (mμ)	$\epsilon_{max.}$
trans-1 : *trans*-5... (I)	110°/0·4	(m. p. 43°)	87°	136—138°/ 4×10^{-2}	(m. p. 52°)	1·91	226	10,800
cis-1 : *trans*-5 (II)	105°/0·15	1·4718	58°	128°/8 × 10^{-4}	1·4830	1·98	226	9,400
trans-1 : *cis*-5 (III)	94—95°/ 8×10^{-2}	1·4746	45°	141°/5 × 10^{-2}	1·4836	1·86	226	10,700
cis-1 : *cis*-5 (IV) [1]	—	—	—	125—126°/ 5×10^{-4}	1·4856	—	227 [2]	10,300 [2]

[1] Data of Raphael and Sondheimer (*loc. cit.*). [2] Supplementary data.
* Adjusted to 20° by −0·0004 per degree within a range of ±5°.
† Double bonds determined by microhydrogenation.

A similar regularity was noted in the *S*-benzylthiuronium salts of the four geometrically isomeric undeca-1 : 7-diene-1-carboxylic acids in Part I.

Useful confirmation of the structure and stereochemistry of the four diene-*iso*butylamides springs from an interpretation of their infra-red spectra (see Figure). All four compounds show the N–H stretching frequency (3302—3293 cm.$^{-1}$) with the amide B absorption in the position expected for a monosubstituted amide (1555—1551 cm.$^{-1}$); the small band characteristic of amides at 3076 cm.$^{-1}$ is present. The position of the amide A absorption (1634—1631 cm.$^{-1}$, compared with 1644 cm.$^{-1}$ for *N-iso*butylnonane-1-carboxyamide) indicates the αβ-unsaturation. This is further confirmed by ultra-violet light absorption data (Table) which accord with previous observations (Part I).

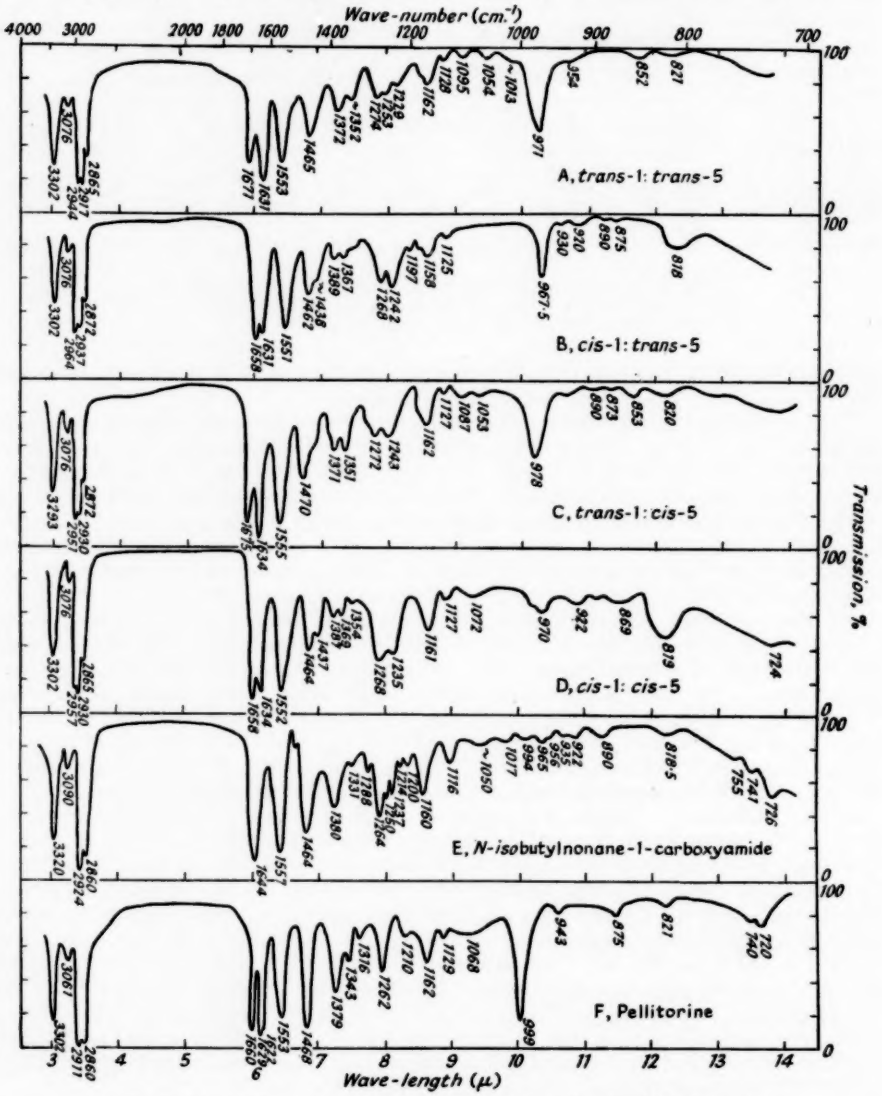
In Part I certain observations were made on the relation of geometrical stereochemistry to the infra-red absorption in the olefinic=C—H out-of-plane deformation region and in the C=C stretching region. The results obtained here may be interpreted along similar lines. The two isomers with *cis*-αβ-double bonds have the C=C stretching frequency at a lower value (1658 cm.$^{-1}$) than the *trans* (1675 and 1671 cm.$^{-1}$). In the region involving the deformation frequency of hydrogen atoms attached to an ethylenic linkage (Rasmussen, Brattain, and Zuco, *J. Chem. Physics*, 1947, **15**, 135; see also Part I), the *cis*-1 : *trans*-5- has absorption at lower frequencies (967·5 cm.$^{-1}$) than the *trans*-1 : *cis*-5-compound (978 cm.$^{-1}$). All this is as expected. The *cis-cis*-isomer shows some absorption in the latter region which is probably due to contamination with stereoisomers, arising because it is produced by partial catalytic (palladium) hydrogenation of a diyne (the extent of contamination, however, seems qualitatively greater than in the undeca-1 : 7-diene-1-carboxyamide series). Observations on *N-iso*butylnona-*trans*-1 : *trans*-5-diene-1-carboxyamide were somewhat disappointing; in the undeca-1 : 7-diene series two bands were resolved at 964·5 and 977 cm.$^{-1}$ due to the αβ- and the γδ-double bonds respectively, but for the nonadiene only one band was obtained though its shape indicates that two unresolved bands are probably present. It is interesting that the qualitative fluctuations of intensity in the band at *ca.* 820 cm.$^{-1}$ and the two between 1230 and 1280 cm.$^{-1}$ (all of which are also present in the saturated analogue) parallel in this series of stereoisomers those observed in the undeca-1 : 7-diene series (Part I).

Since the general stereochemical assignments to the four *N-iso*butylnonadiene-1-carboxyamides can be accepted with some assurance, their relation to pellitorine may be examined. Direct comparison with a specimen of natural pellitorine, m. p. 73° (infra-red spectrum *F*), isolated from the root of *Anacyclus pyrethrum* showed that none was identical with it. Further, unlike pellitorine, they were comparatively stable substances and had low insecticidal potencies. Although they had a bitter taste and (particularly the

trans-1 : *cis*-5-isomer) some sialogogue activity these were not comparable with those of pellitorine. Jacobson's structure for pellitorine must be incorrect.

The situation therefore resembles that reached in Part I concerning Jacobson's structure

Infra-red spectra of N-isobutylnona-1 : 5-diene-1-carboxyamides *and related compounds.*



B—D, *Liquid films*; A, E, F, *paraffin mulls, paraffin absorption present.*

for herculin. However, there is one difference. Dr. Jacobson has kindly supplied the author with a sample of his natural pellitorine which on crystallisation had m. p. 73—74°. This was identical with the above specimen (mixed m. p.). We are thus certainly investigating the same material in this case.

Experimental

The ultra-violet light absorption data (in pure ethanol) were obtained by Mrs. I. M. Boston using a Hilger medium quartz instrument. Most of the analytical data and micro-hydrogenations are due to Mr. Oliver of the microanalytical laboratories of this College. The infra-red spectra were measured by the author on a single-beam instrument (see Part I) using liquid films or paraffin mulls; facilities for these measurements were kindly afforded by Dr. W. C. Price.

3-Chlorotetrahydro-2-n-propylfuran.—To a Grignard reagent prepared from magnesium (64 g.) and *n*-propyl bromide (328 g.) in anhydrous ether (600 ml.), cooled to 0°, freshly distilled 2 : 3-dichlorotetrahydropyran (250 g.) (Crombie and Harper, *J.*, 1950, 1714) diluted with an equal volume of ether was added slowly and with good stirring (particularly towards the end of the reaction when solid may separate). The reaction was controlled initially by cooling in ice but the temperature was later allowed to rise to that of the room. Next morning, ammonium chloride solution was added and as much of the ethereal layer as possible decanted. Sufficient concentrated hydrochloric acid was added to dissolve the basic magnesium halide (this caused some resinification) and the solution extracted with ether. The united ethereal solutions were washed with water and dried (K_2CO_3–Na_2SO_4). Removal of the ether and distillation (Dufton column) gave, after elimination of a small fore-run, *cis-* + *trans*-3-chlorotetrahydro-2-*n*-propyl furan (221 g., 83%), b. p. 65—80°/18 mm. (majority 74—77°). Normant (*Compt. rend.*, 1948, **226**, 733) gives b. p. 68—70°/12 mm.

Hept-3-enol.—Sodium (75 g.) was powdered under hot xylene, the xylene decanted, and the residue washed five times with ether. The metal was suspended in ether (700 ml.) and a few drops of 3-chlorotetrahydro-2-*n*-propylfuran were added. After a few minutes a vigorous reaction set in and the remainder of the chloro-compound (221 g. in all) was added dropwise at such a rate that steady refluxing was maintained. The surface of the sodium assumed a deep blue-purple colour. The product was set aside for 12 hours and then decomposed with water. Removal of the ethereal layer and extraction of the aqueous phase with ether gave a pale yellow solution which was washed and dried (Na_2SO_4). Distillation yielded hept-3-enol, b. p. 81—83°/19 mm., n_D^{20} 1·4425 (147·5 g., 87%) (presumed to be a mixture of *cis-* and *trans*-forms). Normant (*loc. cit.*) records b. p. 73°/12 mm. The *p*-diphenylylurethane (after one crystallisation) softened at 84° and melted at 87—92° to a turbid melt which cleared at 96°. On recrystallisation it had m. p. 97° after softening.

Hept-3-ynol.—(a) *Dehydrohalogenation procedure.* Bromine (185 g.) was added during 2 hours to hept-3-enol (132 g.) in ether (150 ml.) with vigorous stirring and cooling in ethanol–solid carbon dioxide (*ca.* 20°). The ether was then evaporated *in vacuo*. A solution of sodamide (from sodium, 100 g.; ferric nitrate, 2 g.) in liquid ammonia (2·5 l.) (Vaughn, Vogt, and Niewland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120) was treated rapidly with the 3 : 4-dibromoheptanol and the mixture stirred for a further 5 hours; ether (200 ml.) was added and the ammonia allowed to evaporate overnight; decomposition with water, extraction with ether (6 × 100 ml.), and distillation yielded crude hept-3-ynol (55·5 g., 42%), b. p. 86—111°/20 mm., n_D^{20} 1·4590, contaminated with monobromohept-3-enol. Fractionation gave pure hept-3-ynol (30 g., 23%), b. p. 86—88°/18 mm., n_D^{20} 1·4537.

(b) *From acetylene.* Sodium (46 g.) was added to liquid ammonia (2 l.) through which acetylene was passing at such a rate that a blue colour did not develop throughout the solution, whilst on the other hand a *considerable* excess of acetylene was never present. Towards the end of the reaction the blue colour was allowed to develop and just removed with acetylene by " titration " (Sondheimer, *J.*, 1950, 877). *n*-Propyl iodide (325 g.) in ether (300 ml.) was added dropwise and the product stirred for 4 hours. Then a solution of sodamide (from sodium 46 g., and liquid ammonia, 1·5 l.) was added and the whole stirred overnight. Excess of ethylene oxide (220 g.) was added in one portion and the mixture stirred for 30 hours. After addition of ether the excess of ammonia was allowed to evaporate and the residue decomposed with dilute hydrochloric acid. Extraction with ether and fractionation of the product (Stedman column) gave hept-3-yn-1-ol (48·6 g., 23%), b. p. 117—120°/83 mm., n_D^{20} 1·4550. Its 3 : 5-dinitrobenzoate crystallised from light petroleum in needles, m. p. 62°. Newman and Wotiz (*J. Amer. Chem. Soc.*, 1949, **71**, 1292) obtained a 30% yield from pentynylsodium and ethylene oxide in liquid ammonia, and report b. p. 111°/70 mm., n_D^{25} 1·4530, and a 3 : 5-dinitrobenzoate of m. p. 61°.

Ca. 70 g. of material of b. p. 240—242° were also isolated. Its infra-red spectrum indicated the presence of a primary hydroxyl grouping (3250 cm.$^{-1}$, broad; 1054 cm.$^{-1}$, medium-strong), a C≡C linkage situated internally (2222 cm.$^{-1}$, weak) and an ether linkage (1122 cm.$^{-1}$, strong).

Persistently low analyses for carbon were obtained (Found: C, 68·25, 68·15, 68·25; H, 10·3, 10·15, 10·25. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). Microhydrogenation: 1·84 H_2. The p-*diphenylylurethane* crystallised from light petroleum (b. p. 60—80) in prisms, m. p. 88 (Found: C, 74·75; H, 7·35. $C_{22}H_{25}O_2N$ requires C, 75·2; H, 7·15%). A 3 : 5-*dinitrobenzoate* was also prepared, of m. p. 62° [needles from light petroleum (b. p. 40—60°)] (Found: C, 54·65; H, 4·85. $C_{16}H_{18}O_7N_2$ requires C, 54·85; H, 5·2%). Its appearance differed from that of the 3 : 5-dinitrobenzoate of hept-3-ynol (m. p. 62°) and on admixture the m. p. was depressed (partly melted 45°; turbid liquid 50°). It seems that the yield of hept-3-ynol could be considerably increased by using less ethylene oxide in this preparation.

trans-n-*Hept-3-en-1-ol*.—Hept-3-ynol (20 g.) was added in ether (25 ml.) to a solution of sodium (20 g.) in liquid ammonia (600 ml.) and stirred for 2 hours. After the addition of an excess of ammonium chloride, ether (50 ml.) was added and the ammonia evaporated. Water was added and the ethereal layer separated, washed, and distilled, to yield trans-n-*hept-3-en-1-ol* (17·2 g., 84%), b. p. 170—171°, n_D^{20} 1·4415 (Found: C, 74·1; H, 12·45. $C_7H_{14}O$ requires C, 73·6; H, 12·35%). The p-*diphenylylurethane* crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 105° (Found: C, 77·6; H, 7·6. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·4%).

trans-n-*Hept-3-enyl Bromide*.—Phosphorus tribromide (4·0 ml.) was added to a mixture of *trans*-hept-3-enol (13·0 g.) and pyridine (2·0 ml.) with stirring and cooling in ice. After stirring (30 minutes) the crude bromide was distilled directly from the flask at 100 mm. (b. p. 105—140°) and worked up as described for the *cis*-isomer (below). Distillation gave trans-n-*hept-3-enyl bromide* (13·2 g., 57·5%), b. p. 169—179°; on redistillation the main portion had b. p. 172—175°, n_D^{25} 1·4641 (Found: Br, 44·65. $C_7H_{13}Br$ requires Br, 45·15%).

trans-*Oct-4-enal*.—A Grignard reagent, prepared from *trans*-hept-3-enyl bromide (10·4 g.) and magnesium (1·4 g.) in ether (25 ml.) was treated with ethyl orthoformate (8·8 g.) and refluxed for 3·5 hours. The mixture was worked up as described for the *cis*-isomer and gave *trans*-oct-4-enal (2·75 g., 40%), b. p. 173°, n_D^{20} 1·4360 (Found: C, 76·15; H, 11·1. Calc. for $C_8H_{14}O$: C, 76·1; H, 11·2%). The 2 : 4-dinitrophenylhydrazone crystallised from ethanol in long golden-yellow needles, m. p. 110° (Found: C, 55·3; H, 6·2; N, 18·2. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9; N, 18·3%). Jacobson (*loc. cit.*) gave b. p. 80—84°/13 mm., n_D^{25} 1·4463; 2 : 4-dinitrophenylhydrazone, m. p. 108°.

Nona-trans-1 : trans-5-*diene*-1-*carboxylic Acid*.—*trans*-Oct-4-enal (1·26 g.) was set aside with malonic acid (1·04 g.) and pyridine (1·0 ml.) for 4 days. All the solid had dissolved with effervescence and the mixture was then heated on the steam-bath for 2 hours to complete decarboxylation. Isolation of the acid (0·80 g., 48%) was effected as described for the *trans*-1-*cis*-5-isomer. The acid crystallised from the distillate in plates which, when dried between filter papers, had m. p. 42—43°. Jacobson (*loc. cit.*) records m. p. 35°.

The p-*bromophenacyl* ester formed plates (from ethanol–water), m. p. 87° (Found: C, 58·9; H, 6·05. $C_{18}H_{21}O_3Br$ requires C, 59·2; H, 5·8%). For further data see Table.

N-iso*Butyl*-trans-1 : trans-5-*diene*-1-*carboxyamide*.—The *trans-trans*-acid (350 mg.) was treated with thionyl chloride (0·25 ml.) and set aside for 90 minutes. The crude acid chloride was diluted with benzene (3 ml.), and excess of *iso*butylamine (0·8 ml.) added with cooling. Working up in the usual way and distilling gave the *trans-trans-iso*butylamide (262 mg., 63%), needles, m. p. 52°; when admixed with the specimen kindly supplied by Dr. Jacobson (m. p. 53—54°) its m. p. was raised to 53—54°. For further data see Table.

cis-*Hept-3-enol*.—Hept-3-ynol (23·5 g.) was hydrogenated without a solvent in the presence of 3% palladium–calcium carbonate until 4·5 l. of hydrogen had been absorbed (1 mol., 4·7 l.; volumes corrected to N.T.P.). Ether and filter-cel were added and the catalyst filtered off. cis-*Hept-3-enol*, isolated by distillation, had b. p. 80—82°/18 mm., n_D^{20} 1·4435 (22·0 g., 92%) (Found: C, 73·85; H, 12·75. $C_7H_{14}O$ requires C, 73·6; H, 12·35%). The p-*diphenylurethane* crystallised from light petroleum (b. p. 80—100°) as needles, m. p. 84—85° (Found: C, 78·05; H, 7·55. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·4%).

cis-*Hept-3-enyl Bromide*.—*cis*-Hept-3-enol (20·5 g.) was cooled in ice, and pyridine (4·1 ml.) added. Phosphorus tribromide (19·5 g.) was then added dropwise with stirring during 1·5 hours and the mixture allowed to warm to room temperature and left for a further hour. The crude bromide was isolated by direct distillation at 210 mm. (31·6 g.). It was washed with 10% sodium hydroxide solution, 10% hydrochloric acid, and water, separations being aided by the addition of light petroleum (b. p. 40—60°). cis-*Hept-3-enyl bromide*, isolated by removal of the solvent and distillation (26·6 g., 79%), had b. p. 68—72°/15 mm., n_D^{20} 1·4705 (Found: C, 47·8; H, 7·65. $C_7H_{13}Br$ requires C, 47·5; H, 7·4%).

cis-*Oct-4-enal*.—A Grignard reagent was prepared from *cis*-hept-3-enyl bromide (25·0 g.) and

magnesium (3·3 g.) in ether (40 ml.). After 20 minutes' refluxing freshly distilled ethyl orthoformate (20 g.; b. p. 146—148°) was added to the cooled reagent, the mixture refluxed for a further 6 hours, and the ether then distilled. Ice-cold 6% hydrochloric acid was added (90 ml.) and the emulsion which resulted was broken by the addition of 6% sulphuric acid (100 ml.). The upper acetal layer was separated. Steam-distillation of the aqueous acid phase showed that the amount of acetal or aldehyde contained in it was quite small.

The acetal was steam-distilled with 4% sulphuric acid (200 ml.), and the crude volatile aldehyde collected and purified by shaking it with sodium metabisulphite (20 g.) in water (60 ml.). Traces of undissolved material were rejected. cis-*Oct-4-en-1-al* (8·8 g., 58%), liberated by the addition of excess of sodium hydrogen carbonate and steam-distilled, had b. p. 173°, n_D^{20} 1·4353 (Found : C, 75·3; H, 11·15. $C_8H_{14}O$ requires C, 76·1; H, 11·2%). The **2 : 4-***dinitrophenylhydrazone* crystallised in yellow needles (from ethanol), m. p. 81° (Found : C, 54·65; H, 6·1; N, 17·7. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%).

Nona-trans-1 : cis-5-*diene*-1-*carboxylic Acid.*—*cis*-Oct-4-enal (4·2 g.) was added to an ice-cooled mixture of malonic acid (3·47 g.) and anhydrous pyridine (3·2 ml.). Two liquid phases were formed and much malonic acid remained undissolved. After 40 hours at room temperature the mixture became homogeneous; it was then heated for 2 hours on a water-bath. The product was cooled, acidified with 50% ice-cold sulphuric acid (Congo-red), and the acidic and the neutral material were isolated with light petroleum (b. p. 40—60°). The petroleum solution was thoroughly extracted with aqueous sodium hydrogen carbonate. The acid was liberated from the aqueous phase by just acidifying it under light petroleum (b. p. 40—60°). Drying (Na_2SO_4) and removal of the petroleum gave *nona*-trans-1 : cis-5-*diene*-1-*carboxylic acid* (2·32 g., 59%) (Found : C, 72·0; H, 9·85. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). A white to buff polymer fairly soluble in ether, remained in the distillation flask. The acid was characterised as its p-*bromophenacyl* ester which crystallised from ethanol–water as needles, m. p. 44—45° (Found : C, 59·4; H, 5·95%).

Nona-trans-1 : cis-5-*diene*-1-*carboxyl Chloride.*—Thionyl chloride (1·40 g.) was added slowly to nona-*trans*-1 : *cis*-5-diene-1-carboxylic acid (1·50 g.) and set aside overnight. Removal of the excess of thionyl chloride under vacuum and distillation gave the *acid chloride* (1·47 g., 88%), b. p. 118°/16 mm., n_D^{20} 1·4817 (Found : C, 64·4; H, 8·25; Cl, 19·75. $C_{10}H_{15}OCl$ requires C, 64·3; H, 8·1; Cl, 19·0%).

N-iso*Butylnona*-trans-1 : cis-5-*diene*-1-*carboxyamide.*—To the *trans*-1 : *cis*-5-acid chloride, (1·03 g.) in light petroleum (b. p. 40—60°) redistilled *iso*butylamine (1·00 g.) was added slowly. The solution was washed with water, dried, and evaporated, and the residue distilled, to give the required iso*butylamide*, as an almost colourless and rather viscous liquid (1·13 g., 92%) (Found : C, 75·0; H, 11·55; N, 6·05. $C_{14}H_{25}ON$ requires C, 75·25; H, 11·3; N, 6·25%).

trans-*Nona*-5-*ene*-1-*yne*-1-*carboxylic Acid.*—A Grignard reagent was prepared from propargyl bromide (23·0 g.; Kirrmann, *Bull. Soc. chim.*, 1926, **39**, 698) and magnesium (4·6 g.) in ether (60 ml.) a little mercuric chloride being used to start the reaction. It was cooled to 20° and *trans*-hex-2-enyl bromide (28·5 g.; Bouis, *Ann. Chim.*, 1928, **9**, 403) in ether (30 ml.) added dropwise. This caused gentle refluxing and two phases formed. The product was set aside for 18 hours, refluxed for 1 hour, cooled, and decomposed with water (vigorous reaction) followed by dilute hydrochloric acid. The ethereal layer was separated, the aqueous phases extracted, and the united ethereal extracts were dried and distilled. Six fractions were collected : (1) b. p. 55—105°, n_D^{21} 1·4430 (2·0 g.); (2) b. p. 105—125°, n_D^{21} 1·4541 (2·0 g.); (3) b. p. 125—136°, n_D^{21} 1·4528 (2·5 g.); (4) b. p. 136—141°, n_D^{21} 1·4520 (2·8 g.); (5) b. p. 141—144°, n_D^{21} 1·4522 (11·9 g. Found : Br, 23·6%); (6) temperature falling, n_D^{21} 1·4568 (2·1 g.). Fractions (2)—(4) and the first runnings of (5) were turbid, but slowly cleared. Fractions (4) and (5) were bulked and used below (Found : C, 67·3; H, 9·1; Br, 22·9%). Infra-red spectral examination showed a sharp band (medium-strong) at 3290 cm.$^{-1}$ (−C≡CH), a weak band at 2110 cm.$^{-1}$ attributable to the acetylenic carbon–carbon stretching frequency in an R·C≡CH environment, and the internal *trans*-olefin frequency (966 cm.$^{-1}$, strong). Johnson and McEwen's reagent gave a turbidity (yellow-green) with only slight precipitation, changing to greyish (cf. *trans*-undeca-7-ene-1-yne, Part I). Another preparation yielded crude material of b. p. 148—150°, n_D^{21} 1·4436.

The crude coupling product (13·1 g.) was added to a Grignard reagent prepared from ethyl bromide (23·4 g.) and magnesium (5·16 g.) in ether and refluxed for 4 hours. It was then sealed in an autoclave with a large excess of solid carbon dioxide for 18 hours. Decomposition with dilute hydrochloric acid, purification through sodium hydroxide solution in the usual way, and distillation yielded trans-*non*-5-*ene*-1-*yne*-1-*carboxylic acid* (6·2 g., 25% overall), b. p. 109—111°/0·2 mm., n_D^{20} 1·4778 (Found : C, 72·05; H, 8·6. $C_{10}H_{14}O_2$ requires C, 72·25; H, 8·5%).

Its p-*bromophenacyl* ester crystallised from ethanol in plates or needles, m. p. 82° (Found : C, 59·4; H, 5·5. $C_{18}H_{19}O_3Br$ requires C, 59·6; H, 5·3%).

Hydrogenation of the enyne-acid yielded a product which rapidly solidified (m. p. 31°). The m. p. was undepressed in admixture with authentic nonane-1-carboxylic acid (m. p. 31·5°).

Nona-cis-1 : trans-5-*diene*-1-*carboxylic Acid*.—The enyne-acid (1·57 g.) were hydrogenated in ethyl acetate over palladium–calcium carbonate until 220 ml. of gas was absorbed (1 mol. = 226 ml. at 20°/764 mm.). Filtration and distillation yielded the required *acid* (1·43 g.), n_D^{17} 1·4730 (Found : C, 71·0; H, 9·6%). Crystallisation of its p-*bromophenacyl* ester gave plates (from ethanol–water), m. p. 58° (Found : C, 58·6; H, 5·8%).

N-iso*Butylnona*-cis-1 : trans-5-*diene*-1-*carboxyamide*.—The above acid (850 mg.) was heated under reflux with oxalyl chloride (1·5 ml.) in benzene (5 ml.) for 1 hour and the solvent and excess of reagent were removed *in vacuo* at 20°. More benzene (3 ml.) was added and the process repeated. The crude acid chloride was diluted with ether and the *amide* prepared as described above. On distillation it (85%) had $n_D^{22\cdot5}$ 1·4820 (Found : C, 75·2; H, 11·0; N, 6·0%). The material did not crystallise.

A second specimen was made from *trans-N-iso*butylnon-5-en-1-yne-1-carboxyamide. The latter (b. p. 138°/4 × 10^{-3} mm., n_D^{23} 1·4858) was prepared by the oxalyl chloride method and semihydrogenated in the usual way, to give the *cis*-1 : *trans*-5-*iso*butylamide (n_D^{22} 1·4780, $\lambda_{max.}$ 227 mμ; $\varepsilon_{max.}$ 8250). It was probably less pure than the other specimen. During the preparation of the enyne-*iso*butylamide colourless needles were isolated which were almost insoluble in light petroleum (b. p. 40—60°) but crystallised readily from ethanol and then had m. p. 170° (Found : C, 59·9; H, 10·25. Calc. for $C_{10}H_{20}O_2N_2$: C, 59·95; H, 10·05%). It is the di*iso*butylamide of oxalic acid, indicating that the excess of oxalyl chloride had not been completely removed. Chablay (*Ann. Chim.*, 1914, **1**, 495) gives m. p. 169°.

Insecticidal Tests.—These were carried out through the kindness of Dr. C. Potter by Mr. M. Elliott and Mr. P. Needham of the Department of Insecticides and Fungicides, Rothamsted Experimental Station. Application of 0·004 ml. of the acetone solutions (below) was made dorsally between the prothorax and the mesothorax to adults of *Tenebrio molitor* (male and female). The results were as follows :

	Concn. (%, w/v)	Kill (%)		Concn. (%, w/v)	Kill (%)
trans-1 : *trans*-5	1·92	4	*cis*-1 : *cis*-5	2·64	8
cis-1 : *trans*-5	2·02	0	Natural pellitorine [1]	1·17	88
trans-1 : *cis*-5	1·92	4			

[1] Crude specimen, m. p. 59—63°.

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831. *The Scope of the Knoevenagel Synthesis of Aromatic Secondary Amines.*

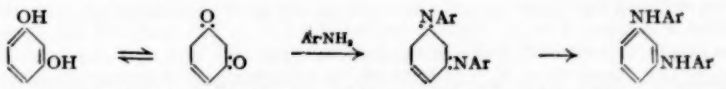
By NG. PH. BUU-HOÏ.

Knoevenagel's method for preparing aromatic secondary amines by iodine-catalysed condensation of hydroxy-compounds with aromatic amines has been extended, as regards the phenolic component, to several polyhydric benzene and naphthalene derivatives and to 6-bromo-2-naphthol, and, as regards the amino-component, to a series of substituted anilines and to 2-aminopyridine. Attempts to synthesise *N-cyclo*alkyl-β-naphthylamines resulted chiefly in di-β-naphthylamine, in contrast to statements in the literature.

THE varied synthetical use in our Laboratory of aromatic secondary and tertiary amines warranted a broad investigation into methods for their preparation. Knoevenagel (*J. prakt. Chem.*, 1914, **89**, 1) found that α- and β-naphthol reacted readily with aniline and its homologues in the presence of small amounts of iodine, to yield α-aryl-α- and -β-naphthylamines. It has now been found that resorcinol and anilíne or *p*-toluidine similarly give good yields of 1 : 3-dianilino- and 1 : 3-di-*p*-toluidino-benzene. *o*- and *p*-Diphenols were less reactive, as quinol and *p*-toluidine gave a mixture of much 5-hydroxy-4'-methyldiphenyl-

amine and a little 1 : 4-di-*p*-toluidinobenzene (the yield of the latter was raised slightly by prolonged heating), and catechol gave only small amounts of diamine. Quinol also gave predominantly a hydroxy-diphenylamine with, *e.g.*, *m*-toluidine, 2 : 4-dimethylaniline, and *p*-anisidine.

The present procedure for the preparation of hydroxydiarylamines and 1 : 3- and 1 : 4-diarylaminobenzenes is far more convenient than those which involve the use of dehydrating agents (Calm, *Ber.*, 1883, **16**, 2794, 2805; Philip and Calm, *Ber.*, 1884, **17**, 2431; Hatschek and Zega, *J. prakt. Chem.*, 1886, **33**, 209, 230; Philip, *ibid.*, 1886, **34**, 70) or mineral acids (Bradfield, Cooper, and Orton, *J.*, 1927, 2856). The difference in the reactivity of the three dihydric phenols suggests that the Knoevenagel amination process involves the formation of *N*-arylketimines with rearrangement to arylamines. For resorcinol the sequence of reaction would be :



From that viewpoint, phloroglucinol, a substance with pronounced ketonic properties, should be highly reactive; as thus expected, it gave, even on brief heating, the 1 : 3 : 5-trisarylaminobenzenes listed in Table 1.

Knoevenagel (*loc. cit.*) readily obtained 2 : 3- and 2 : 7-dianilinonaphthalene from aniline and 2 : 3- and 2 : 7-dihydroxynaphthalene respectively. This observation has now been extended to several other arylamines and to 1 : 6- and 2 : 6-dihydroxynaphthalene (for the new products see Table 2). Whereas both 1-chloro-2-naphthol and 2-chloro-1-naphthol were completely dehalogenated on condensation with aniline in the presence of iodine (Knoevenagel, *loc. cit.*), the bromine atom in 6-bromo-2-naphthol has now been found to resist the action of aniline and *p*-toluidine, 6-bromo-*N*-phenyl- and -*p*-tolyl-2-naphthylamine being readily obtained. An attempt to prepare *N-cyclo*hexyl-β-naphthylamine from β-naphthylamine and *cyclo*hexanol in the presence of iodine yielded only di-β-naphthylamine (by the action of iodine on β-naphthylamine alone; cf. Knoevenagel, *loc. cit.*, and Butterworth and Hey, *J.*, 1940, 388). Di-β-naphthylamine was also obtained as sole secondary amine when β-naphthylamine was heated with *cyclo*hexyl bromide, 3-methyl*cyclo*hexyl bromide, or *cyclo*heptyl bromide; Loevenich, Utsch, Moldrickx, and Schaefer (*Ber.*, 1929, **62**, 3097) held that in those reactions *N-cyclo*hexyl-, *N*-3-methyl-*cyclo*hexyl-, and *N-cyclo*heptyl-β-naphthylamine were formed, but from the melting points it seems that their products were di-β-naphthylamine in different degrees of purity.

The Knoevenagel synthesis of secondary amines could be extended to the heterocyclic group : 2-aminopyridine readily gave 2-α- and 2-β-naphthylaminopyridine (of interest as intermediates for the synthesis of antihistamines) which had hitherto been prepared less conveniently (Fischer, *Ber.*, 1902, **35**, 3674).

Experimental

Condensation of 2-Aminopyridine with Naphthols.—A mixture of β-naphthol (10 g.), redistilled 2-aminopyridine (10 g.), and iodine (0·2 g.) was refluxed for 24 hours; the mixture was taken up in benzene, and the benzene solution washed with aqueous sodium hydroxide, then with water, and dried (Na_2SO_4); removal of the solvent and vacuum-fractionation of the residue gave 2-β-naphthylaminopyridine (75%), b. p. *ca.* 245—250°/15 mm., prisms, m. p. 135° (from benzene–*cyclo*hexane) (lit., 133°). Similarly, α-naphthol gave 2-α-naphthylaminopyridine (60%), prisms, m. p. 116° (from benzene–*cyclo*hexane) (lit., 115°).

Attempted Synthesis of N-cyclo*Hexyl-β-naphthylamine.*—(*a*) A mixture of *cyclo*hexyl bromide (25 g.) and β-naphthylamine (40 g.) was refluxed for 2 hours; the product, which contained much *cyclo*hexene, was washed with dilute aqueous ammonia and taken up in benzene; vacuum-fractionation yielded di-β-naphthylamine (8 g.), leaflets (from ethanol), m. p. 172° alone or mixed with an authentic sample (Knoevenagel, *loc. cit.*). Similar results were recorded when *cyclo*hexyl bromide was replaced by 3-methyl*cyclo*hexyl or *cyclo*heptyl bromide, or simply 48% hydrobromic acid (10 c.c.). (*b*) *cyclo*Hexanol (20 g.), β-naphthylamine (40 g.), and iodine (0·2 g.) were heated for 10 hours at 230—240° (cf. Knoevenagel's preparation of *N-iso*amylaniline, *loc. cit.*); di-β-naphthylamine, m. p. 172°, was the only product isolated.

6-*Bromo*-N-*phenyl*-2-*naphthylamine*.—6-Bromo-2-naphthol (7 g.), aniline (20 g.), and iodine (0·1 g.) were gently refluxed for 20 hours with removal of the water formed. The mixture was treated with dilute hydrochloric acid, and the solid product washed with cold methanol and recrystallised from ethanol, to give the secondary amine as prisms (10 g.), m. p. 126° (Found: C, 64·2; H, 4·1. $C_{16}H_{12}NBr$ requires C, 64·4; H, 4·4%); the picrate formed, from ethanol, brown-violet needles, m. p. 125°.

6-*Bromo*-N-p-*tolyl*-2-*naphthylamine* crystallised from ethanol as leaflets, m. p. 157° (Found: C, 65·3; H, 4·6. $C_{17}H_{14}NBr$ requires C, 65·4; H, 4·5%), giving a brown-violet picrate.

Condensation of Resorcinol with Arylamines.—Resorcinol (25 g.), *p*-toluidine (60 g.), and iodine (1 g.) were refluxed for 3 days. Working up in the usual way gave **1 : 3-di-*p*-toluidinobenzene** (20 g.), crystallising from ethanol as prisms, m. p. 139°; the same reaction with aniline gave **1 : 3-dianilinobenzene**, m. p. 96°, in lower yield (15 g.).

Condensation of Quinol with the Toluidines.—(*a*) Quinol (10 g.), *p*-toluidine (25 g.), and iodine (0·5 g.) were refluxed for 3 days, and the mixture worked up in the usual way; vacuum-fractionation yielded **4-hydroxy-4′-methyldiphenylamine** (9 g.), b. p. 238—240°/15 mm., prisms, m. p. 119° (from ligroin, b. p. 80—100°) (Hatschek and Zega, *loc. cit.*), and **1 : 4-di-*p*-toluidinobenzene** (2·5 g.), m. p. 182° (from ethanol). (*b*) Similarly ***m*-toluidine** gave **4-*hydroxy*-3′-*methyldiphenylamine*** (11 g.), b. p. 232—234°/15 mm., needles, m. p. 61—62° (from ligroin) (Found: C, 78·2; H, 6·6. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5%); the portion of b. p. >260°/15 mm. yielded, on crystallisation from ethanol, **1 : 3-*di*-m-*toluidinobenzene*** (2 g.), leaflets, m. p. 112° (Found: C, 83·1; H, 7·2. $C_{20}H_{20}N_2$ requires C, 83·3; H, 6·9%).

Condensation of Quinol with **2 : 4-*Dimethylaniline*.**—Quinol (10 g.), **2 : 4-dimethylaniline** (25 g.), and iodine (0·25 g.) were refluxed for 48 hours, to yield **4-*hydroxy*-2′ : 4′-*dimethyldiphenylamine*** (10 g.), b. p. 235—238°/14 mm., prisms, m. p. 85—86° (from ligroin, b. p. 80—100°) (Found: C, 78·7; H, 7·1. $C_{14}H_{15}ON$ requires C, 78·9; H, 7·0%), and **1 : 3-*di*-(2 : 4-*dimethylanilino*)*benzene*** (2 g.), b. p. >280°/15 mm., needles (from ethanol), m. p. 120° (Found: C, 83·2; H, 7·8. $C_{22}H_{24}N_2$ requires C, 83·5; H, 7·6%).

Condensation of Quinol with **p-*Anisidine*.**—Quinol (10 g.), *p*-anisidine (25 g.), and iodine (0·25 g.) yielded, after 48 hours, **4-*hydroxy*-4′-*methoxydiphenylamine*** (10 g.), b. p. 245—248°/14 mm., leaflets (from ligroin, b. p. as above), m. p. 93° (Found: C, 72·4; H, 6·0. $C_{13}H_{13}O_2N$

TABLE 1. **1 : 3 : 5-*Trisarylaminobenzenes*.**

Aryl group	M. p.	Formula	Found, % C	Found, % H	Required, % C	Required, % H
Ph [a]	196°	$C_{24}H_{21}N_3$	—	—	—	—
o-C_6H_4Me	157	$C_{27}H_{27}N_3$	82·2	7·2	82·4	6·9
m-C_6H_4Me	133	$C_{27}H_{27}N_3$	82·5	6·8	82·4	6·9
p-C_6H_4Cl	226	$C_{24}H_{18}N_3Cl_3$	63·0	4·2	63·4	4·0
2 : 3 : 1-C_6H_3ClMe	164	$C_{27}H_{24}N_3Cl_3$	65·1	5·0	65·3	4·8
2 : 4 : 1-$C_6H_3Me_2$	150	$C_{30}H_{33}N_3$	82·5	7·5	82·8	7·6
p-$CMe_2Et{\cdot}C_6H_4$	159	$C_{39}H_{51}N_3$	83·1	9·2	83·4	9·1
o-$MeO{\cdot}C_6H_4$	139	$C_{27}H_{27}O_3N_3$	73·3	6·3	73·5	6·1
p-$MeO{\cdot}C_6H_4$	167	$C_{27}H_{27}O_3N_3$	73·6	6·2	73·5	6·1
o-C_6H_4Ph	173	$C_{42}H_{33}N_3$	86·7	5·5	87·0	5·7
p-C_6H_4Ph [b]	252	$C_{42}H_{33}N_3$	87·2	5·5	87·0	5·7
α-$C_{10}H_7$	227	$C_{36}H_{27}N_3$	86·0	5·6	86·2	5·4

[a] Minunni (*Gazzetta*, 1890, **20**, 237) gave m. p. 193°. [b] Recrystallised from benzene; almost insoluble in ethanol.

TABLE 2. *Bisarylaminonaphthalenes.*

Substituents	M. p.	Formula	Found, % C	Found, % H	Required, % C	Required, % H
1 : 6-Dianilino	164°	$C_{22}H_{18}N_2$	85·0	6·0	85·2	5·8
1 : 6-Di-*p*-toluidino	146	$C_{24}H_{22}N_2$	85·1	6·3	85·2	6·5
1 : 6-Di-(2 : 4-dimethylanilino)	103	$C_{26}H_{26}N_2$	85·0	7·4	85·2	7·1
1 : 6-Di-*p*-methoxyanilino	183	$C_{24}H_{22}O_2N_2$	77·5	6·1	77·8	5·9
2 : 7- ,,	176	$C_{24}H_{22}O_2N_2$	77·6	6·2	77·8	5·9
2 : 7-Di-*p*-hydroxyanilino [a]	243—245° [b]	$C_{22}H_{18}O_2N_2$	76·9	5·4	77·2	5·2
2 : 7-Di-β-naphthylamino	253—255° [b]	$C_{30}H_{22}N_2$	89·0	5·4	88·7	5·4
2 : 6-Di-*p*-toluidino	193	$C_{24}H_{22}N_2$	85·2	6·6	85·2	6·5
2 : 6-Di-*o*-toluidino	183	$C_{24}H_{22}N_2$	85·0	6·5	85·2	6·5
2 : 6-Di-α-naphthylamino	212° [b]	$C_{30}H_{22}N_2$	88·9	5·2	88·7	5·4

[a] All substances were recrystallised from ethanol–benzene, except this which was recrystallised from aqueous ethanol. [b] With decomp.

requires C, 72·6; H, 6·0%), and 1 : 3-*di*-p-*anisidinobenzene* (12 g.), leaflets (from benzene), m. p. 189° (Found : C, 74·8; H, 6·2. $C_{20}H_{20}O_2N_2$ requires C, 75·0; H, 6·3%).

Condensation of Phloroglucinol and Dihydroxynaphthalenes with Arylamines.—(*a*) Phloroglucinol (1 mol.), the arylamine (4—5 mols.), and iodine (2%) were heated at 190—200° for 6 hours with removal of water; the warm product was treated with methanol, and the solid obtained washed thoroughly with the same solvent and recrystallised from ethanol or benzene. The 1 : 3 : 5-*trisarylaminobenzenes* (Table I) thus obtained in almost theoretical yield were needles or leaflets. (*b*) In the case of dihydroxynaphthalenes, purification of the *products* (Table 2) in most instances required vacuum-distillation before crystallisation.

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832. *A Synthesis of* 3 : 4-*Dimethyl* D-*Xylose and* 4-*Methyl* D-*Xylose.*

By L. HOUGH and J. K. N. JONES

3 : 4-Dimethyl D-xylose and 4-methyl D-xylose have been synthesised from D-arabinose *via* 2 : 3-anhydro-β-methyl-D-riboside. Crystalline derivatives suitable for their characterisation are described.

3 : 4-DIMETHYL D-XYLOSE has been reported to occur in the fission products of methylated tragacanthic acid (James and Smith, *J.*, 1945, 739), of methylated mucilages (Mullan and Percival, *J.*, 1940, 1501; Nelson and Percival, *J.*, 1942, 99), and of a methylated aldobiuronic acid, namely, 2-(4-methyl D-glucuronopyranosyl)-D-xylose, obtained from aspen wood (Jones and Wise, *J.*, 1952, 3389). We attempted the synthesis of this xylose derivative since it was not well characterised and a synthesis described by Robertson and Speedie (*J.*, 1934, 825) is ambiguous. 2 : 3-Anhydro-β-methyl-D-riboside (Honeyman, *J.*, 1946, 990; Kent, Stacey, and Wiggins, *J.*, 1949, 1234) was prepared from D-arabinose and methylated by Purdie's reagents to give a readily crystallised 4-methyl derivative. Treatment of the latter with sodium methoxide gave a dimethyl methylpentoside. As expected from the results of Honeyman (*loc. cit.*), Mukherjee and Todd (*J.*, 1947, 969), and Kent, Stacey, and Wiggins (*loc. cit.*), the product contained largely 3 : 4-dimethyl-β-methyl-D-xyloside and not the arabinose derivative. Proof of identity was obtained by methylation to 2 : 3 : 4-trimethyl β-methyl-D-xyloside which on hydrolysis gave 2 : 3 : 4-trimethyl D-xylose. Hydrolysis of 3 : 4-dimethyl methylxyloside gave 3 : 4-dimethyl D-xylose as a syrup, which gave a crystalline xylosylamine derivative and lactone. Recently, we became aware of an independent synthesis by another route of 3 : 4-dimethyl D-xylose by Percival and Zobrist and, through the kindness of Dr. E. E. Percival, details of this work appear concurrently with this publication. We have compared samples and, from mixed m. p. data and paper chromatograms, the products are clearly identical and resemble those described by James and Smith (*loc. cit.*).

Aqueous alkaline hydrolysis of 4-methyl 2 : 3-anhydro-β-methyl-D-riboside afforded crystalline 4-methyl β-methyl-D-xyloside. The methylglycoside consumed one mol. of periodate, gave 2 : 3 : 4-trimethyl β-methyl-D-xyloside on methylation, and depressed the melting point of 2-methyl β-methyl-D-xyloside. Acidic hydrolysis of the methylglycoside gave syrupy 4-methyl D-xylose which was converted into the crystalline osazone.

EXPERIMENTAL

M. p.s are uncorrected. Microanalyses are by Mr. B. S. Noyes of Bristol. Evaporations were carried out under reduced pressure.

4-*Methyl* 2 : 3-*Anhydro*-β-*methyl*-D-*riboside.*—β-Methyl-D-arabinoside (4·8 g.) was converted into the 3 : 4-*iso*propylidene derivative by Honeyman's method (*loc. cit.*). The crude product (5·4 g.) was treated in pyridine (25 c.c.) with toluene-*p*-sulphonyl chloride (7 g.). After 24 hours at 20°, the solution was poured on ice, and the precipitate of crude 3 : 4-*iso*propylidene 2-toluene-*p*-sulphonyl β-methyl-D-arabinoside was recrystallised from aqueous ethanol. The product (7·8 g.), m. p. 136°, was dissolved in boiling acetone (25 c.c.), and the *iso*propylidene residue removed by addition of 0·1N-formic acid (50 c.c.), during 2 hours. Evaporation of the solvent afforded syrupy 2-toluene-*p*-sulphonyl β-methyl-D-arabinoside (4·4 g.), which was dissolved in

methanol containing sodium methoxide (from 1 g. of sodium). Overnight, sodium toluene-*p*-sulphonate separated. It was filtered off, and the filtrate was diluted with water, neutralised with sulphuric acid (phenolphthalein), and extracted continuously with chloroform. Concentration of the chloroform extract yielded syrupy 2 : 3-anhydro-β-methyl-D-riboside (2·2 g.). This material was methylated by two treatments with silver oxide and methyl iodide with the formation of crystalline 4-*methyl* 2 : 3-*anhydro*-β-*methyl*-D-*riboside* (2·2 g.) which on recrystallisation from light petroleum (b. p. 40—60°) gave long needles, m. p. 75—77°, $[\alpha]_D^{19}$ −7° (*c*, 1·49 in water) (Found : C, 52·8; H, 7·3; OMe, 38·8. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5; OMe, 38·8%). The product sublimes at 90—100°.

3 : 4-*Dimethyl* β-*Methyl*-D-*xyloside*.—The latter anhydro-compound (0·7 g.) was heated in methanol (25 c.c.) containing sodium (1·5 g.) for 24 hours. The solution was evaporated to a small volume, diluted with water, and extracted continuously with chloroform. Evaporation of the extract gave crystals (0·7 g.) of 3 : 4-*dimethyl* β-*methyl*-D-*xyloside*, which on recrystallisation from ether–light petroleum (b. p. 40—60°) had m. p. 89—90°, not depressed on admixture with a sample provided by Dr. E. E. Percival, $[\alpha]_D^{19}$ −71° (*c*, 1·53 in water) (Found : C, 49·8; H, 8·0; OMe, 48·3. $C_8H_{16}O_5$ requires C, 50·0; H, 8·3; OMe, 48·4%).

Methylation of a portion (0·15 g.) of this substance with Purdie's reagents gave 2 : 3 : 4-trimethyl β-methyl-D-xyloside (0·14 g.), m. p. and mixed, m. p. 47—48°, $[\alpha]_D^{19}$ −68·5° (*c*, 1·36 in chloroform), after recrystallisation from light petroleum (b. p. 40—60°). Acid hydrolysis in the usual manner gave 2 : 3 : 4-trimethyl D-xylose, which was isolated on a tile and recrystallised from ether–light petroleum (b. p. 40—60°), then having m. p. and mixed m. p. 89—90°, $[\alpha]_D^{21}$ +46° ⟶ −24° (constant; *c*, 0·67 in chloroform) (Found : OMe, 46·9. Calc. for $C_8H_{16}O_5$: OMe, 48·4%).

3 : 4-*Dimethyl* D-*Xylose*.—3 : 4-Dimethyl β-methyl-D-xyloside was hydrolysed with hydrochloric acid (0·5N) on the boiling-water bath for 12 hours ($[\alpha]_D$ +12° at equilibrium). The solution was neutralised with silver carbonate, then filtered, and the solution concentrated to syrupy 3 : 4-dimethyl D-xylose (0·53 g.), $[\alpha]_D$ +13° (*c*, 1·6 in methanol) (Found : OMe, 34·7. Calc. for $C_7H_{14}O_5$: OMe, 34·8%), which moved at the same rate on paper chromatograms, in a variety of solvents, as did authentic 3 : 4-dimethyl D-xylose (for details see Jones and Wise, *loc. cit.*). A portion of the syrup (96 mg.) was heated under reflux with alcoholic aniline for 1 hour, and on removal of the solvent a crystalline xylosylamine derivative was formed. This material was unstable, rapidly darkening in the air, and was difficult to purify by recrystallisation. It was purified by partition chromatography on Whatman No. 1 paper, with *n*-butanol–ethanol–water (40 : 11 : 19) as mobile phase. The xylosylamine derivative, which was detected by using the *p*-anisidine hydrochloride spray reagent (Hough, Jones, and Wadman, *J.*, 1950, 1702), moved at a slower rate than the coloured impurities and aniline, and faster than 3 : 4-dimethyl D-xylose. Extraction of the appropriate section of the paper chromatogram yielded *N*-phenyl-D-xylosylamine 3 : 4-dimethyl ether, m. p. 126° and mixed m. p. 124° with a specimen previously prepared (Jones and Wise, *loc. cit.*).

3 : 4-*Dimethyl* D-*Xylonolactone*.—3 : 4-Dimethyl D-xylose (0·33 g.) was oxidised with bromine water at about 30° for 48 hours, and the product isolated in the usual way, to give 3 : 4-dimethyl D-xylonolactone (0·21 g.) which crystallised spontaneously. After recrystallisation from ether, it had $[\alpha]_D^{16}$ −50° (10 mins.; *c*, 1·1 in water) ⟶ −22° (48 hours, constant), m. p. 68°, undepressed on admixture with samples prepared by Jones and Wise (*loc. cit.*) and Dr. E. E. Percival (personal communication) (Found : C, 47·7; H, 6·8; OMe, 35·5. Calc. for $C_7H_{10}O_5$: C, 47·7; H, 6·8; OMe, 35·2%). The derived *phenylhydrazide* had m. p. 132° (Found : C, 54·9; H, 7·0; N, 10·2; OMe, 22·7. $C_{13}H_{20}O_5N_2$ requires C, 54·9; H, 7·0; N, 9·9; OMe, 21·8%).

4-*Methyl* β-*Methyl*-D-*xyloside*.—4-Methyl 2 : 3-anhydro-β-methyl-D-riboside (0·25 g.) was heated with sodium hydroxide (5%; 25 c.c.) on the boiling-water bath for 48 hours. Initially, a bright yellow colour formed, and slowly disappeared. The cooled solution was neutralised with sulphuric acid and extracted exhaustively with chloroform. Concentration of the extract gave crystals of 4-*methyl* β-*methyl*-D-*xyloside* (0·16 g.), m. p. 95° after recrystallisation from ether ($[\alpha]_D^{22}$ −69°; *c*, 0·44 in water) (Found : OMe, 34·7. $C_7H_{14}O_5$ requires OMe, 34·8%). Methylation of a portion (55 mg.) with Purdie's reagents gave 2 : 3 : 4-trimethyl β-methyl-D-xyloside, m. p. and mixed m. p. 46—47°, $[\alpha]_D^{20}$ −66° (*c*, 0·78 in methanol). A further portion (20·8 mg.) in water (5 c.c.) was left with 0·2M-sodium metaperiodate (1 c.c.) in the dark for 24 hours; then the solution (pH 5·0) was treated with saturated solution of sodium hydrogen carbonate and 0·1N-sodium arsenite (5 c.c.). After 0·5 hour, the solution was titrated with 0·01N-iodine (25·5 c.c.) (Found : 1 mole of metaperiodate is consumed by 163 g. of the methylxyloside. $C_7H_{14}O_5$ requires the consumption of 1 mole per 178 g. of the xyloside).

4-Methyl D-*Xylose*.—The methylglycoside (44 mg.) was hydrolysed with N-sulphuric acid (20 c.c.) for 6 hours. Then the solution was cooled and neutralised with barium carbonate in the usual way. Evaporation gave syrupy *4-methyl* D-*xylose* {39 mg.; $[\alpha]_D$ +9° ± 2° (*c*, 0·66 in water)}. On paper chromatograms, using Whatman No. 1 paper, its rate of movement relative to that of rhamnose was 1·22, 1·11, and 1·28 with (*a*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), (*b*) *n*-butanol–pyridine–water (10 : 3 : 3), and (*c*) *n*-butanol–ethanol–water (40 : 11 : 19) as mobile phase. Solvents (*b*) and (*c*) separate 4-methyl from 2-methyl xylose (rates of movement, 1·43 and 1·24 respectively) and with *p*-anisidine hydrochloride as spray reagent show different colours, a reddish-brown and a mauve respectively.

4-Methyl D-*xylosazone* was prepared by heating the sugar (35 mg.) in water (5 c.c.) with phenylhydrazine (0·2 c.c.) and glacial acetic acid (0·2 c.c.) at *ca.* 70° for 3 hours. The reaction mixture was cooled to 2°, and the crystalline osazone filtered off and recrystallised from methanol–water. After drying, it had m. p. 160—161° (Found : OMe, 9·0. $C_{18}H_{22}O_3N_4$ requires OMe, 9·1%).

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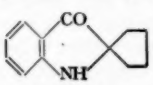
833. *Peroxides of Tetrahydrocarbazole and Related Compounds. Part III.* A Synthesis of* 5 : 6-*Dimethoxy*cyclo*pentane*spiro-2-ψ-*indoxyl.*

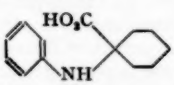
By R. J. S. BEER, T. BROADHURST, ALEXANDER ROBERTSON, and (in part) L. MCGRATH.

5 : 6-Dimethoxy*cyclo*pentane*spiro*-2-ψ-indoxyl (VI) was obtained from 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxycarbazolyl hydroperoxide by way of the corresponding hydroxycarbazolenine (VII; R = OH), and was identical with a specimen prepared by cyclisation of (V) which was synthesised from (IV), when R = H, NO_2, NH_2, and NHAc, successively.

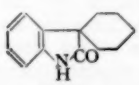
THE decomposition of 1 : 2 : 3 : 4-tetrahydrocarbazolyl hydroperoxide under a variety of conditions has been shown to give *cyclo*pentane*spiro*-2-ψ-indoxyl (I) (Part I, *J.*, 1950, 2118), the structure of which has been the subject of discussion (Plant and Robinson, *Nature*, 1950, **165**, 36; Witkop, *J. Amer. Chem. Soc.*, 1950, **72**, 614). Although there are substantial reasons for believing that the indoxyl is correctly formulated, the only direct synthetical evidence is that of Plant and Robinson (*loc. cit.*) who, in a preliminary account, describe the preparation of the compound, evidently in low yield, by the alkylation of *N*-acetylindoxyl with 1-bromo-4-chloro-*n*-butane and sodamide. Earlier attempts to synthesise compounds similar to (I) by cyclisation of acids of type (II) gave products which are now recognised as *cyclo*hexane*spiro*oxindoles, type (III) (see, *e.g.*, Moore and Plant, *J.*, 1951, 3475), whilst the alkaline fusion of 1-anilino*cyclo*pentane-1-carboxylic acid gave carbazole (Plant and Facer, *J.*, 1925, **127**, 2037).



(I)



(II)

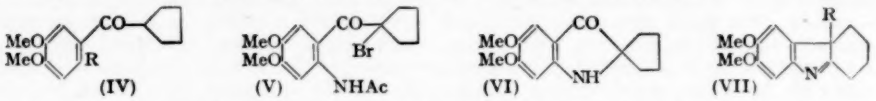


(III)

It appeared to us that application of Baeyer's synthesis of indoxyl from *o*-acetamido-ω-bromoacetophenone (*Ber.*, 1884, **17**, 963) might provide a rational route to *spiro*-ψ-indoxyls of type (I). For the synthesis of the parent *spiro*-2-ψ-indoxyl (I), the preparation of the required intermediate *o*-nitrophenyl *cyclo*pentyl ketone presents considerable difficulties, but nitration of the corresponding veratrole derivative (IV; R = H) was expected to furnish (IV; R = NO_2) required for 5 : 6-dimethoxy*cyclo*pentane*spiro*-2-ψ-indoxyl (VI), which had already been prepared in this laboratory from 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxycarbazolyl hydroperoxide (VII; R = O·OH) (*Nature*, 1949, **164**, 362). This peroxide closely resembled 1 : 2 : 3 : 4-tetrahydrocarbazolyl hydroperoxide (Part I, *loc. cit.*) and on reduction with aqueous sodium sulphite gave 11-hydroxy-6 : 7-

* Part II, *J.*, 1950, 3283.

dimethoxycarbazolenine (VII; R = OH) which, with warm aqueous sodium hydroxide, rearranged to the *spiro*-2-ψ-indoxyl (VI) having the expected properties.



Accordingly, 3 : 4-dimethoxyphenyl *cyclo*pentyl ketone was prepared from veratrole and *cyclo*pentanecarboxyl chloride by the Friedel–Crafts method and, on nitration, gave a moderate yield of a mononitro-derivative, which was shown by the ultimate success of the synthesis to be 4 : 5-dimethoxy-2-nitrophenyl *cyclo*pentyl ketone (IV; R = NO_2) and on catalytic reduction furnished 2-amino-4 : 5-dimethoxyphenyl *cyclo*pentyl ketone (IV; R = NH_2), forming the acetyl derivative (IV; R = NHAc). *N*-Bromosuccinimide did not react with this acetamido-ketone but, after some preliminary experiments, the compound was found to react satisfactorily with bromine in acetic acid to give (V). With warm aqueous sodium hydroxide this product (V) was smoothly converted into 5 : 6-dimethoxy*cyclo*pentane*spiro*-2-ψ-indoxyl, identical with the specimen previously prepared, thus confirming the structures assigned to this class of compound.

Experimental

3 : 4-*Dimethoxyphenyl* cyclo*Pentyl Ketone* (IV; R = H).—Powdered aluminium chloride (4·0 g.) was added to a solution of veratrole (5·7 g.) and *cyclo*pentanecarboxyl chloride (Haworth and Perkin, *J.*, 1894, **65**, 99) (5·7 g.) in carbon disulphide (20 ml.), and 2 hours later the deep red mixture was added to crushed ice (50 g.) and concentrated hydrochloric acid (20 ml.). On isolation with ether (washing successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water) the resulting 3 : 4-*dimethoxyphenyl* cyclo*pentyl ketone* was purified by distillation and obtained as a colourless mobile oil (6·2 g.) which slowly solidified to a mass of needles, b. p. 122—124°/0·05 mm., m. p. 39—40° (Found : C, 71·8; H, 7·7. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). The 2 : 4-*dinitrophenylhydrazone*, which formed slowly in boiling alcohol, separated in minute shining plates, m. p. 162°, on recrystallisation from alcohol (Found : C, 58·4; H, 5·4; N, 13·2. $C_{20}H_{22}O_6N_4$ requires C, 58·0; H, 5·4; N, 13·5%). Under the usual conditions the ketone did not form an oxime or a semicarbazone.

4 : 5-*Dimethoxy*-2-*nitrophenyl* cyclo*Pentyl Ketone* (IV; R = NO_2).—A solution of the foregoing ketone (2·5 g.) in acetic acid (2 ml.) was added during 10 minutes to a well-stirred mixture of concentrated nitric acid (6·5 ml.) and concentrated sulphuric acid (2·8 ml.) at −5°. When the mixture was poured into ice-water (75 ml.) 10 minutes later, a red resin separated which slowly solidified and then, on crystallisation from methanol, gave 4 : 5-*dimethoxy*-2-*nitrophenyl* cyclo*pentyl ketone* (1·6 g.) in clusters of colourless rods, m. p. 97—98° (Found : C, 60·6; H, 5·9; N, 5·2. $C_{14}H_{17}O_5N$ requires C, 60·2; H, 6·1; N, 5·0%). This compound did not react with the usual carbonyl reagents.

2-*Acetamido*-4 : 5-*dimethoxyphenyl* cyclo*Pentyl Ketone* (IV; R = NHAc).—Reduction of the nitro-ketone (IV; R = NO_2) (2·0 g.), dissolved in methanol (100 ml.), with hydrogen at atmospheric pressure and a palladium–charcoal catalyst was complete in 2 hours and, on evaporation of the filtered solution, gave the amino-ketone as a pale green crystalline mass which was directly converted into the *acetyl* derivative with acetic anhydride (4 ml.) on the steam-bath for 1 hour. This compound separated from light petroleum (b. p. 60—80°) in colourless prisms (1·5 g.), m. p. 112°, which did not react with carbonyl reagents (Found : C, 66·1; H, 7·2; N, 5·0. $C_{16}H_{21}O_4N$ requires C, 66·0; H, 7·2; N, 4·8%).

2-*Acetamido*-4 : 5-*dimethoxyphenyl* 1-*Bromo*cyclo*pentyl Ketone* (V).—On the addition of bromine (0·3 g.) in acetic acid (0·5 ml.) to a solution of 2-acetamido-4 : 5-dimethoxyphenyl *cyclo*pentyl ketone (0·5 g.) in the same solvent (3 ml.) at 50°, hydrogen bromide was evolved and the *bromo-ketone* (V) separated in minute yellow prisms (0·6 g.). Recrystallised from aqueous alcohol, the ketone formed short golden-yellow rods, m. p. 146° (decomp.) (Found : C, 52·1; H, 5·4; N, 3·7. $C_{16}H_{20}O_4NBr$ requires C, 52·0; H, 5·4; N, 3·8%).

5 : 6-*Dimethoxy*-2-cyclo*pentane*spiro-ψ-*indoxyl*.—(*a*) On being heated on the steam-bath for 2 hours with 2N-aqueous sodium hydroxide (2 ml.) the foregoing bromo-ketone (V) (0·1 g.) gave 5 : 6-*dimethoxy*cyclo*pentane*spiro-2-ψ-*indoxyl*, which formed pale green prisms (55 mg.), m. p. 164—165°, from light petroleum (b. p. 60—80°) (Found : C, 68·4; H, 7·0; N, 5·7. $C_{14}H_{17}O_3N$ requires C, 68·0; H, 6·9; N, 5·7%).

(*b*) When a solution of 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxycarbazole (Hughes and Lions, *J. Proc. Roy. Soc., N.S. Wales*, **1938**, **71**, 428) (1·5 g.) in light petroleum (b. p. 60—80°) (700 ml.) was kept overnight, the hydroperoxide separated in colourless prisms (1·3 g.), m. p. *ca.* 113° (decomp.), and on recrystallisation from ethyl acetate–light petroleum had m. p. *ca.* 122° (decomp.) [cf. *Nature*, **1949**, **164**, 362, where m. p. 118° (decomp.) is recorded]. A mixture of the hydroperoxide (0·8 g.), 30% aqueous sodium sulphite (20 ml.), and ether (120 ml.) was agitated for 4 hours, and the product, 11-hydroxy-6 : 7-dimethoxycarbazolenine (0·30 g.), m. p. 158°, isolated with ether. When this crude compound (0·25 g.) was heated on the steam-bath with a solution of potassium hydroxide (0·5 g.) in ethanol (3 ml.) and water (2 ml.) for 30 minutes, and the alcohol subsequently removed by distillation, 5 : 6-dimethoxy-2-*cyclo*pentane*spiro*-ψ-indoxyl (0·21 g.) separated and, on crystallisation from benzene–light petroleum, formed green elongated prisms, m. p. 165°, undepressed by admixture with the sample obtained by route (*a*) (Found : C, 68·1; H, 6·7; N, 5·7%).

The two samples had identical absorption spectra in alcohol (Light absorption : Max. at 252, 277, and 390 mμ; log ε = 4·35, 4·09, and 3·78).

UNIVERSITY OF LIVERPOOL. [*Received, July 29th*, 1952.]

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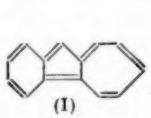
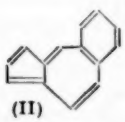
834. *Cyclic Conjugated Polyenes. The Attempted Synthesis of Dehydroindeno(5′ : 6′-1 : 2)cyclo*heptatriene.

By A. D. CAMPBELL and S. N. SLATER.

Cyclisation of δ-5-indanylvaleric acid gives indano(5′ : 6′-1 : 2)*cyclo*hepten-3-one which is oxidised by selenium dioxide to indano(5′ : 6′-1 : 2)*cyclo*heptene-3 : 4-dione and this on dehydrogenation gives indano(5′ : 6′-α : β)-tropolone. Attempts to dehydrogenate indano(5′ : 6′-1 : 2)*cyclo*hepta-1 : 3-diene, *tricyclo*[7 : 5 : $0^{3:7}$]tetradecane, indano(5′ : 6′-1 : 2)*cyclo*heptene, and 3-methylindano(5′ : 6′-1 : 2)*cyclo*hepta-1 : 3-diene, all prepared from the above monoketone, were unsuccessful.

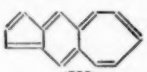
THE existence of the azulenes has served as an incentive in the search for such analogous compounds as pentalene and heptalene but neither of these two substances has yet been prepared. In the azulene series, 1 : 2-benzazulene (I) (Plattner, Fürst, Chopin, and Winteler, *Helv. Chim. Acta*, **1948**, **31**, 501; Treibs, *Angew. Chem.*, **1947**, **59**, 244; *Ber.*, **1948**, **81**, 39; Nunn and Rapson, *J.*, **1949**, 825), and 5 : 6-benzazulene (II) (Plattner, Fürst, and Keller, *Helv. Chim. Acta*, **1949**, **32**, 2464) are known and Nunn and Rapson (*J.*, **1949**, 1051) have prepared a trinitrobenzene complex of 4 : 5-benzazulene (III) although the hydrocarbon itself could not be isolated.


(I)

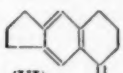

(II)

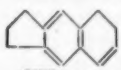
(III)

The present communication describes some attempts to prepare dehydroindeno(5′ : 6′-1 : 2)*cyclo*heptatriene (IV) in which the azulene system has been extended by an intermediate six-membered ring. The first route investigated was from 2 : 3-*cyclo*pentenonaphthalene (V) or 5 : 6 : 7 : 8-tetrahydro-5-keto-2 : 3-*cyclo*pentenonaphthalene (VI) (Sen Gupta, *Current Sci.*, **1936**, **5**, 133). The most satisfactory preparation of (VI), obtained by cyclis-


(IV)

(V)


(VI)


(VII)

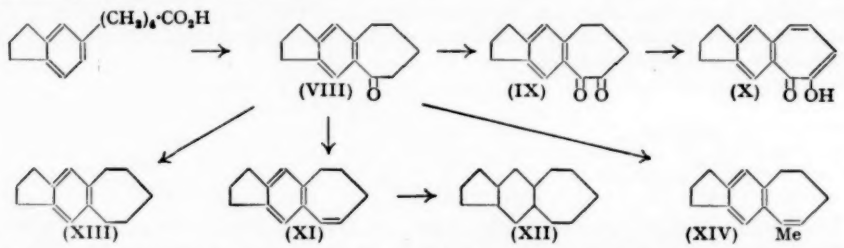
ation of γ-5-indanylbutyric acid, was achieved through use of anhydrous hydrogen fluoride as cyclising agent. Although Nunn and Rapson (*loc. cit.*) were successful in enlarging the *cyclo*hexanone ring of 1 : 2 : 3 : 4 : 10 : 11-hexahydrofluoren-3-one with diazomethane, (VI) failed to react with diazomethane even when the latter was generated in the reaction

mixture (Kohler, Tishler, Potter, and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 1059). The expansion of one of the six-membered rings of fluorene by diazoacetic ester has been described by Plattner *et al.*, by Nunn and Rapson, and by Treibs (*locc. cit.*). A very small yield of condensation product was obtained from (V) and diazoacetic ester, but 5 : 6-dihydro-2 : 3-*cyclo*pentenonaphthalene (VII), obtained from (VI) by reduction with sodium and ethanol and dehydration of the resulting alcohol, reacted with diazoacetic ester to give, after hydrolysis, a crude nitrogen-free acid. This was dehydrogenated with palladium–charcoal and activated alumina. The product was purple, and from it by chromatographic adsorption a small amount of a deep-blue semi-solid was isolated. An attempt to form a trinitrotoluene complex resulted in polymerisation.

The Demjanov reaction provides an alternative method of ring expansion (Plattner, Fürst, and Studer, *Helv. Chim. Acta*, 1947, **30**, 1091) but the necessary methylamino-compound could not be prepared. Hydrogen cyanide failed to react with (VI), and the corresponding alcohol gave only a low yield of the bromide which readily formed (VII) during the attempted preparation of the cyanide.

The next attempt was made from indane by building on a seven-membered ring in a conventional way [indane → δ-5-indanyl-δ-ketovaleric acid → δ-5-indanylvaleric acid → indano(5′ : 6′-1 : 2)*cyclo*hepten-3-one (VIII)]. The position taken up by the entering side-chain in the first reaction was shown by nitric acid oxidation of the product to benzene-1 : 2 : 4-tricarboxylic acid, and the direction of cyclisation by oxidation of the ketone (VIII) to benzene-1 : 2 : 4 : 5-tetracarboxylic acid. The structures of Sen Gupta's products were also confirmed by oxidation of (VI) to the same tetracarboxylic acid. [It should be noted that the trivial names of the benzenetetracarboxylic acids are still a source of confusion in the literature. The correct usage of the trivial names, and the orientation of the acids, is clearly given by Smith and Byrkit (*J. Amer. Chem. Soc.*, 1933, **55**, 4305).]

Oxidation of (VIII) with selenium dioxide gave indano(5′ : 6′-1 : 2)*cyclo*heptene-3 : 4-dione (IX) which was dehydrogenated with palladium–charcoal in boiling trichlorobenzene (Caunt, Crow, Haworth, and Vodoz, *J.*, 1950, 1631) to indano(5′ : 6′-α : β)tropolone (X). A small quantity of the tropolone was also obtained from an oxidation in which the product was distilled from the reaction mixture without previous removal of unchanged selenium dioxide (cf. Borgwardt and Schwenk, *J. Amer. Chem. Soc.*, 1934, **56**, 1185, and Armstrong and Robinson, *J.*, 1934, 1650, for the dehydrogenating action of selenium dioxide). The tropolone gave the usual reactions.



The ketone (VIII) was reduced with sodium and alcohol and the resulting alcohol dehydrated to indano(5′ : 6′-1 : 2)*cyclo*hepta-1 : 3-diene (XI). Because of the possible effect of the degree of hydrogenation on the course of the proposed final dehydrogenation, several related substances were also prepared. Catalytic hydrogenation of (XI) gave the perhydro-derivative *tricyclo*[7 : 5 : $0^{3,7}$]tetradecane (XII), and Clemmensen reduction of (VIII) gave indano(5′ : 6′-1 : 2)*cyclo*heptene (XIII). Methylmagnesium iodide reacted with (VIII) to give the alcohol which lost water on distillation to form 3-methylindano(5′ : 6′-1 : 2)-*cyclo*hepta-1 : 3-diene (XIV).

A wide variety of dehydrogenation techniques (sulphur, selenium, platinum black, palladium–charcoal with and without added solvent, catalytic dehydrogenation in the vapour phase with palladium–charcoal supported on asbestos or with activated alumina, *N*-bromosuccinimide followed by pyridine) was applied to the above substances but in no

case was any indication obtained that the desired product was being formed. In most experiments the starting material was recovered or black polymeric products formed. It may well be that the most energetically favoured system possible within the carbon skeleton examined is that in which the central ring is benzenoid, and that for this reason any attempt to prepare (IV) is unlikely to be successful. The situation is, of course, quite different in (I), (II), and (III) where the presence of the benzenoid ring is not incompatible with the development of the fully conjugated cyclic polyene system.

Experimental

5 : 6 : 7 : 8-*Tetrahydro-5-keto-2* : 3-cyclo*pentenonaphthalene* (VI).—*γ*-5-Indanylbutyric acid (50 g.) and anhydrous hydrogen fluoride (*ca.* 500 g.) were allowed to react for 48 hours. After most of the hydrogen fluoride had evaporated ice was added, and the organic material extracted with ether, washed with water and then aqueous sodium carbonate, dried, and distilled to give the ketone (33 g.), b. p. 190—195°/25 mm. The **2 : 4-*dinitrophenylhydrazone*** formed bright red needles (from much acetic acid), m. p. 258° (decomp.) (Found : N, 15·2. $C_{19}H_{18}O_4N_4$ requires N, 15·3%).

5 : 6 : 7 : 8-*Tetrahydro-5-hydroxy-2* : 3-cyclo*pentenonaphthalene*.—Sodium (10 g.) was added in small portions during 2 hours to the above ketone (4·5 g.) in absolute ethanol (70 c.c.), to give the ***alcohol*** (3·8 g.), b.p. 180—185°/20 mm. (Found : C, 82·7; H, 8·8. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%).

5 : 6-*Dihydro-2* : 3-cyclo*pentenonaphthalene* (VII).—The above alcohol (11 g.) in benzene (20 c.c.) was heated under reflux with phosphoric oxide (13 g.) for 4 hours. The product was poured into water, separated, and distilled, to give the ***hydrocarbon*** (7 g.), b. p. 148—150°/12 mm. (Found : C, 91·4; H, 8·6. $C_{13}H_{14}$ requires C, 91·8; H, 8·2%).

Attempted Ring-enlargement of **5 : 6-*Dihydro-2* : 3-cyclo*pentenonaphthalene***.—5 : 6-Dihydro-2 : 3-*cyclo*pentenonaphthalene (8·5 g.) was heated to 135—140° and ethyl diazoacetate (5·5 g.) added dropwise with stirring. After 6 hours at this temperature the product was cooled, taken up in ethanol, and then heated under reflux with 30% aqueous potassium hydroxide (10 c.c.) for 2 hours. The solution was cooled, filtered, and diluted with water, and the ethanol distilled off. The residual aqueous solution was washed with ether, and the free acid liberated with 2N-hydrochloric acid, taken up in ether, washed with water, and dried. Evaporation of the ether left the crude acid as a brown sticky nitrogen-free mass (1·4 g.). It was heated under reflux with 30% palladium–charcoal (0·5 g.) and activated alumina (3 g.) for 15 minutes and distilled, to give a pale purple liquid (0·3 g.) boiling over a wide range. This was dissolved in ether and washed with aqueous sodium hydroxide and water, and the ether evaporated, to give a purple residue (0·11 g.). Chromatographic analysis of the oil in *cyclo*hexane on alumina yielded a pale-blue zone from which *cyclo*hexane–benzene (1 : 1) eluted a deep-blue semi-solid (*ca.* 1 mg.).

δ-5-*Indanyl-δ-ketovaleric Acid*.—Glutaric anhydride, prepared by heating glutaric acid (25 g.) under reflux with acetic anhydride, in tetrachloroethane (50 c.c.) was added dropwise with stirring to indane (22 g.) in nitrobenzene (50 c.c.) and tetrachloroethane (50 c.c.) containing powdered anhydrous aluminium chloride (57 g.). After 3 hours at room temperature and 15 minutes at 100° the mixture was cooled and poured on ice and hydrochloric acid and then steam-distilled. The residual oil, which solidified on cooling, was filtered off and dissolved in ethanol (charcoal) from which **δ-5-*indanyl-δ-ketovaleric*** acid (30 g.) crystallised as needles, m. p. 103°, after the addition of a small quantity of water (Found : C, 72·1; H, 7·2. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). The ***semicarbazone***, crystallised from ethanol, had m. p. 207° (Found : N, 14·4. $C_{15}H_{19}O_3N_3$ requires N, 14·5%). The **2 : 4-*dinitrophenylhydrazone*** crystallised from ethanol in bright red needles, m. p. 162·5—163° (Found : N, 13·2. $C_{20}H_{20}O_6N_4$ requires N, 13·6%). Nitric acid oxidation of the keto-acid gave benzene-1 : 2 : 4-tricarboxylic acid, m. p. 215°.

δ-5-*Indanylvaleric Acid*.—The above acid (20 g.) was heated under reflux for 8 hours with amalgamated zinc (30 g.), concentrated hydrochloric acid (140 c.c.), water (60 c.c.), toluene (30 c.c.), and acetic acid (5 c.c.). The toluene layer was separated, the aqueous layer was extracted with ether, and the solvents were removed from the combined extracts. The product was dissolved in 2N-sodium hydroxide, washed with ether, and reprecipitated with mineral acid. Recrystallisation from aqueous ethanol gave **δ-5-*indanylvaleric acid*** (17 g.), m. p. 70—71° (Found : C, 76·8; H, 8·2. $C_{14}H_{18}O_2$ requires C, 77·0; H, 8·3%).

Indano*(5′ : 6′-1 : 2)cyclo*hepten*-3-*one (VIII).—The above acid (15 g.) was treated with anhydrous hydrogen fluoride (*ca.* 100 g.). After 24 hours the product was poured on ice, ex-

tracted with ether, and washed well with water and aqueous sodium carbonate. Distillation gave the *ketone* as a clear liquid (12 g.), b. p. 200—203°/16 mm. (Found: C, 83·7; H, 7·9. $C_{14}H_{16}O$ requires C, 84·0; H, 8·0%). The *semicarbazone*, crystallised from ethanol, had m. p. 223° (Found: N, 16·6. $C_{15}H_{19}ON_3$ requires N, 16·3%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in deep red needles, m. p. 182—183° (with previous softening when raised slowly from room temperature) (Found: N, 14·7. $C_{20}H_{20}O_4N_4$ requires N, 14·7%). The ketone (0·5 g.) was oxidized with concentrated nitric acid (10 c.c.) at 100° for 3 hours. After the initial vigorous reaction the excess of nitric acid was removed by a slow stream of air. A little water was added and the evaporation to dryness repeated. The residue crystallised from water in clear crystals, sintering at 235° and giving an indefinite m. p. It was esterified with diazomethane, and the methyl ester crystallised from methanol. Hexagonal plates, m. p. 125°, separated and were followed by needles, m. p. 141°, of tetramethyl benzene-1 : 2 : 4 : 5-tetracarboxylate, identical with the product obtained by esterifying the acid from the oxidation of acetyl-ψ-cumene with alkaline potassium permanganate (Mills, *J.*, 1912, 2191). It was at first thought that the substance, m. p. 125°, might be tetramethyl benzene-1 : 2 : 3 : 4-tetracarboxylate (m .p. 133—135°) which would result from the degradation of the ketone with angular fusion of the three rings, but comparison with an authentic specimen, kindly provided by Dr. D. A. Sutton, National Chemical Research Laboratory, Pretoria, showed no similarity. Hexagonal plates, m. p. 125°, giving no depression with the above material of similar m. p., were also isolated from the products of oxidation of acetyl-ψ-cumene. This substance was not further investigated.

Indano(5′ : 6′-1 : 2)cyclo*heptene*-3 : 4-*dione* (IX).—The above ketone (2 g.) in butanol (30 c.c.) was heated under reflux with powdered selenium dioxide (1·7 g.) for 3 hours. The product was cooled, filtered, dissolved in ether, and washed with sodium hydrogen carbonate solution. Distillation gave the *diketone* (1·5 g.), b. p. 195—200°/3 mm. This was dissolved in acetone, centrifuged to remove selenium, and redistilled (Found: C, 78·2; H, 6·9. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). The 2 : 4 *dinitrophenylhydrazone* crystallised from acetic acid in yellow needles, m. p. 235—236° (Found: N, 13·8. $C_{20}H_{18}O_8N_4$ requires N, 14·2%).

Indano(5′ : 6′-α : β)*tropolone* (X).—(*a*) The diketone (1·2 g.) in 1 : 3 : 5-trichlorobenzene (8 g.) was heated under reflux with palladium–charcoal (0·2 g.; 30%) for 8 hours. The product was diluted with benzene, filtered, and extracted with 2N-sodium hydroxide. The deep yellow alkaline solution was washed with ether and acidified, to give the *tropolone* which crystallised from ethanol in long lemon-yellow crystals (0·08 g.), m. p. 127—128° (Found: C, 78·8, 78·9; H, 5·7, 5·8. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·7%).

(*b*) Indano(5′ : 6′-1 : 2)*cyclo*hepten-3-one (3 g.) in butanol (60 c.c.) was heated under reflux with selenium dioxide (3·0 g.) for 3 hours. The filtered solution (charcoal) was distilled, having b. p. 170—200°/3 mm. After several weeks, brown crystals of the tropolone (0·3 g.) had separated; they had m. p. 127—128° after crystallisation from ethanol (charcoal). Distillation of the liquid from which the brown crystals had separated gave the diketone (0·5 g.), b. p. 200°/3 mm., together with unchanged starting material.

The tropolone gave a red-brown ferric test, a crimson precipitate when coupled with diazotized *p*-toluidine, and a deep yellow colour in concentrated hydrochloric acid, and was resistant to oxidation with concentrated nitric acid. Oxidation with alkaline potassium permanganate gave benzene-1 : 2 : 4 : 5-tetracarboxylic acid (tetramethyl ester, m. p. 141°).

Indano(5′ : 6′-1 : 2)cyclo*hepten*-3-*ol*.—Indano(5′ : 6′-1 : 2)*cyclo*hepten-3-one (6 g.) in absolute ethanol (100 c.c.) was reduced by addition of sodium (10 g.) during 1 hour. The product was poured into water, and the solid material collected and crystallised from aqueous ethanol, to give the *alcohol* (5·5 g.), m. p. 104° (Found: C, 83·4; H, 8·9. $C_{14}H_{18}O$ requires C, 83·2; H, 8·9%).

Indano(5′ : 6′-1 : 2)cyclo*hepta*-1 : 3-*diene* (XI).—The above alcohol (5 g.) was heated with powdered potassium hydrogen sulphate (7 g.) at 180—190° for 2 hours. After cooling, the product was extracted with ether and distilled, to give *indano*(5′ : 6′-1 : 2)cyclo*hepta*-1 : 3-*diene* (3 g.), b. p. 165—168°/17 mm. (Found: C, 90·9; H, 8·7. $C_{14}H_{16}$ requires C, 91·3; H, 8·7%), together with some unchanged starting material.

tricyclo[7 : 5 : $0^{3:7}$]*Tetradecane* (XII).—Indano(5′ : 6′-1 : 2)*cyclo*hepta-1 : 3-diene (10 g.) in acetic acid was hydrogenated at 2 atm. pressure in the presence of Adams's platinum oxide (1·0 g.). After 80 hours no further absorption of hydrogen took place. An oil separated during the hydrogenation. The catalyst was filtered off, and the product poured into water and extracted with ether and *cyclo*hexane. Distillation gave the *hydrocarbon* (8·5 g.) as a clear oily liquid, b. p. 153—155°/15 mm. (Found: C, 87·7; H, 12·2. $C_{14}H_{24}$ requires C, 87·5; H, 12·5%).

Indano(5′ : 6′-1 : 2)cyclo*heptene* (XIII).—Reduction of indano(5′ : 6′-1 : 2)*cyclo*hepten-3-one (11 g.) by the Clemmensen–Martin method for 12 hours yielded the *hydrocarbon* (6 g.) as a clear oil, b. p. 170—172°/16 mm. (Found: C, 89·9; H, 9·4. $C_{14}H_{18}$ requires C, 90·3; H, 9·6%).

3-*Methylindano*(5′ : 6′-1 : 2)cyclo*hepta*-1: 3-*diene* (XIV).—Indano(5′ : 6′-1 : 2)*cyclo*hepten-3-one (4 g.) in anhydrous ether was added slowly with stirring and cooling to methylmagnesium iodide (from magnesium, 1 g., and methyl iodide, 6 g., in anhydrous ether). The mixture was heated under reflux (2 hours) and then set aside (16 hours) before being decomposed and worked up in the usual way. The alcohol lost water when refluxed at 16 mm., to give the *hydrocarbon* (3·5 g.), b. p. 168°/16 mm. (Found: C, 90·5; H, 9·3. $C_{15}H_{18}$ requires C, 90·9; H, 9·1%).

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835. *Separation of the Lanthanons by Ion Exchange. A Comparison of Eluants.*

By R. C. Vickery.

A comparison has been made of the efficiencies of various aliphatic carboxylic acids as eluants in separation of the lanthanons by ion-exchange techniques. This comparison indicates that determinations of stability constants for lanthanon complexes can be used to predict the value of the complex-forming agent in ion-exchange separations. Further, when the exchange resin is in the ammonium form, and when high pH values and low flow rates are employed, ethylenediaminetetra-acetic acid at low concentrations gives separations of the lanthanons which are better than those obtained under comparable conditions by any of the other eluants studied, including citrate solutions. The use of bivalent ions as separating elements in elutions with ethylenediaminetetra-acetic acid has been examined, and with manganese as the separating element this technique has yielded excellent separations of neodymium and praseodymium. Attention is also directed to the necessity of considering molar rather than weight concentrations when comparing eluant efficiencies.

The increasing application of ion-exchange techniques to the separation of the lanthanons and other closely similar cations has led to several fundamental studies on the kinetics of ion exchange. In studies on the lanthanons, however, less attention has been paid to the function of the eluant in these separations. Scattered through the literature are reports on separations obtained with different resins and one or two different eluants but, apart from the studies by Spedding *et al.* on citrate eluants (*J. Amer. Chem. Soc.*, 1947, **69**, 2769, etc.), little systematic work has been done with regard to eluant composition.

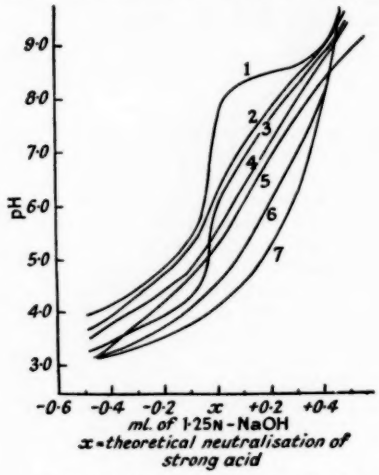
Comparison of the efficiencies of eluants in resin exchange systems may be made in the light of formation and disruption of complexes. Thus the replacement of hydrogen on resins by lanthanons indicates that the lanthanon–resin complexes are more stable than are the hydrogen–resin complexes. Similarly, in the system complex-forming resin–lanthanon ion–complex-forming eluant, the partition of the lanthanon between the resin and the eluant will be proportional to the stabilities of the Ln–resin and Ln–eluant complexes. If the ratio of the stability of a Ln–eluant complex to that of the corresponding Ln–resin complex is denoted by the coefficient A, then the optimum separation of two lanthanon ions will occur when the difference between the two values of A is at its maximum. This is only reached, however, when the system is in equilibrium, *i.e.*, at very slow eluant flow rates. At flow rates employed in practice equilibrium is not attained, but the ratio of coefficients of a lanthanon complex of different eluants may be considered as a measure of their efficiencies at a given approach to equilibrium. This means that an eluant which forms complexes of high stability with the eluted ions will, when employed at

a high flow rate, be approximately as efficient in separation as an eluant affording a low stability, employed at a low flow rate.

Bjerrum has shown (*e.g.*, *Chem. Reviews*, 1950, **46**, 381) that the formation of complex compounds may be treated mathematically so as to yield integrals denoting the overall stabilities of the complexes. However, the nature of the lanthanon complexes with the eluants considered here has not yet been elucidated sufficiently to be amenable to such treatment and the nature of the resin complex systems is even more obscure. But, since it may be accepted that the higher the stability of a complex, the lower the pH at which it can exist, qualitative indications of complex formation and stability may readily be obtained by acid–base titrations of lanthanon systems.

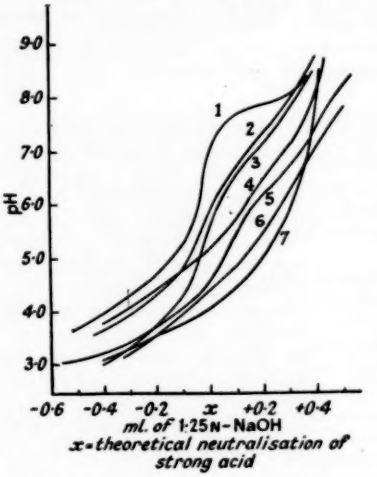
Seven carboxylic acids have been studied for their value as eluants, *viz.*, acetic, malic, tartaric, citric, aminoacetic (glycine), nitrilotriacetic ("trilo"), and ethylenediamine tetra-acetic ("enta"). The pH titration curves for these acids in lanthanon systems are

FIG. 1. *Titrations of* La-*carboxylic acid systems.*



1. Acetic acid.
2. Malic acid.
3. Tartaric acid.
4. Citric acid.
5. Glycine.
6. "Trilo."
7. "Enta."

FIG. 2. *Titrations of* Y-*carboxylic acid systems.*



1. Acetic acid.
2. Malic acid.
3. Tartaric acid.
4. Citric acid.
5. Glycine.
6. "Trilo."
7. "Enta."

given in Figs. 1 and 2, from which is seen an increasing complex stability through the series as listed.

The influence on ion-exchange separations of such factors as eluant flow rate, resin bed depth, resin grain size, etc., have been fully studied by Spedding *et al.* (*loc. cit.*; *Discuss. Faraday Soc.*, No. 7, 1949; U.S.P. 2,539,282/1951). The main variables with different eluants are the exchanging ion, and pH and concentration of eluant. These have been examined for the seven carboxylic acids mentioned above, the cation being ammonium in each case.

Spedding (*loc. cit.*) indicated that, in lanthanon separation by ion exchange, the use of eluants at low concentration and high pH values is of more value, for practical purposes, than at high concentrations and low pH values. Since citrate eluants have been well studied it was decided to consider separations with this as standard. Excellent separations of the lanthanons having been obtained by Spedding using 0·1% citrate solutions at pH 6·0, this eluant concentration was initially employed in these studies but, with each eluant, runs were made in two pH ranges, and with both light and heavy lanthanons adsorbed on Dowex-50 resin.

Typical elution curves have been examined for the eluants studied, all at similar con-

centrations, pH values, and flow rates; those for acetate, citrate, " trilo," and " enta " are given in Figs. 3 and 4. It was immediately evident that (*a*) the efficiency of separation increases with progression through the series to citrate eluants and then decreases, (*b*) higher pH values give best separation of the light lanthanons, and low pH values best of the heavy lanthanons. The latter observation is to be expected from the titration curves of the lanthanon complexes of these acids which show greater difference of the stabilities of the light lanthanon complex series at low pH values. The rise and fall in efficiency of the eluants can be explained on the basis of the argument made above, *viz.*, the lower carboxylic acids, forming lanthanon complexes with stabilities lower than those of the citrate complexes, require a closer approach to equilibrium, *i.e.*, a slower flow rate, in order to approach the efficiency of citrate eluant at the standard flow rate and degree of equilibrium. Similarly, the amino-acids require a faster flow rate as the stabilities of their lanthanon complexes increase.

The elutions with all the acids except " trilo " and " enta " progressed normally, but when these were employed they crystallised in the resin bed when the resin was in its hydrogen form. This was to be expected from the reactions at the adsorption band front :

$$(a) \qquad LnCl_3 + 3HX_{resin} \longrightarrow LnX_{3\ resin} + 3HCl$$

$$(b) \qquad 4HCl + (NH_4)_4\text{"enta"} \longrightarrow 4NH_4Cl + H_4\text{"enta "} \text{ (insoluble)}$$

or $$(b) \qquad 3HCl + (NH_4)_3\text{"trilo"} \longrightarrow 3NH_4Cl + H_3\text{"trilo "} \text{ (insoluble)}$$

The deposition of H_4" enta " in resin columns was noted by Taylor (Univ. Illinois, Thesis, 1950) and by Higgins and Baldwin (ORNL 894, 1951); Taylor reported that " enta " possessed no advantages over citrate as eluant for lanthanons adsorbed on Dowex-50 resin, and considered it to be of value only for " stripping " of the column. Initially, the deposition of H_4" enta " is of value in following the progress of the ion-exchange front, but this front soon outstrips visual observation of the crystallisation. As the concentration of H_4"enta " crystals in the resin bed increases, progressive diminution in eluant flow rate occurs until the adsorption tail passes, thereby making available eluant at a sufficiently high pH for redissolution of the H_4" enta " crystals. The early deposition of H_4" enta " impoverishes the eluant and leads to the falling-off of separation efficiency noted by Taylor. If high concentrations of " enta " are employed in the eluant, operations will eventually be stopped by blocking of the resin column by the deposited crystals.

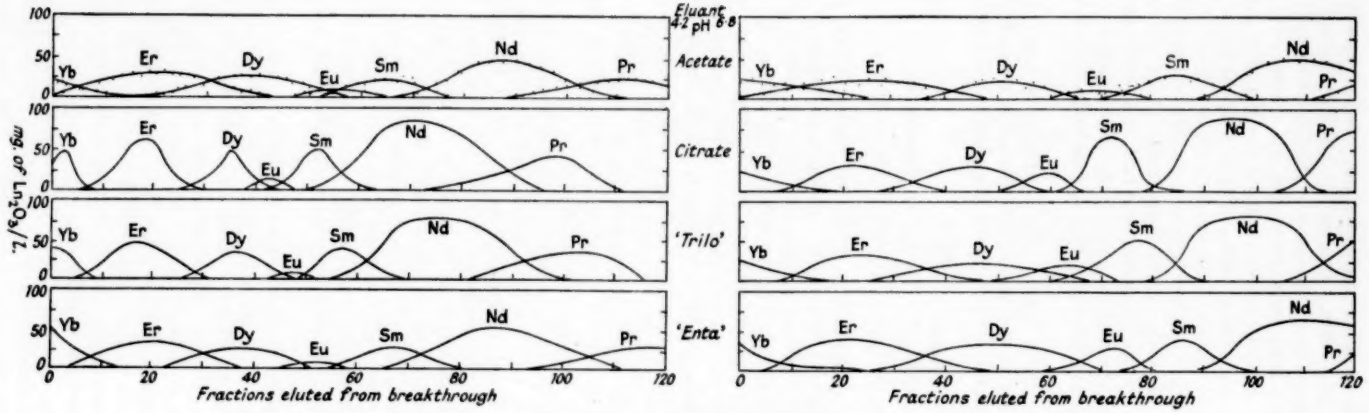
The deposition of H_4" enta " or H_3" trilo " in the resin bed may, however, be avoided by using a resin giving on exchange Na, K, NH_4, or Th, rather than H, ions. However, the elution curves obtained by Ketelle and Boyd (*J. Amer. Chem. Soc.*, 1947, **69**, 2808) show Na to be eluted with the heavy lanthanons; this precludes the use of an exchange resin in the sodium form. On the other hand, thorium would be expected to be too firmly held by the resin to be replaced by lanthanons (Duncan and Lister, *Quart. Reviews*, 1948, **2**, 307). For the separations recorded for " enta " and " trilo " elutions, Dowex-50 in the ammonium form was therefore employed. During progress of this work it was noted that Fitch and Russell (*Canad. J. Chem.*, 1951, **29**, 363) employed resins in the ammonium form during elution of adsorbed lanthanons with " trilo," having also experienced the deposition of the acid in a hydrogen-resin bed.

To confirm the relation of complex stabilities and flow rates, further runs were made with acetate, glycine, and " enta " eluants. The acetate elution was made at a flow rate one-fourth of that of the citrate standard, the glycine elution at a rate 50% higher, and the " enta " elution 100% higher, than the citrate. These runs were made only on a light lanthanon mixture at the higher pH values previously used. Although the acetate elution did not attain the efficiency of the citrate runs, all three eluants showed highly significant increases in efficiencies, particularly the amino-acid eluants which demonstrated a much improved separation over the citrate. The variation in efficiencies is the more significant as the flow rates of the eluants were chosen quite arbitrarily.

Hitherto, in the literature, statements of eluant concentration have been given as a percentage on a w/v basis. In comparing eluant efficiencies, however, this is insufficient, and concentrations should be expressed as molar concentrations. The need for this is

FIG. 3.

FIG. 4.



Elution of mixed lanthanons from Dowex-50 resin by carboxylate solutions at pH *values* 4·2 *and* 6·8.

FIGS. 5 & 6. *Elution of light lanthanons by "enta" at higher concentration and flow rate.*

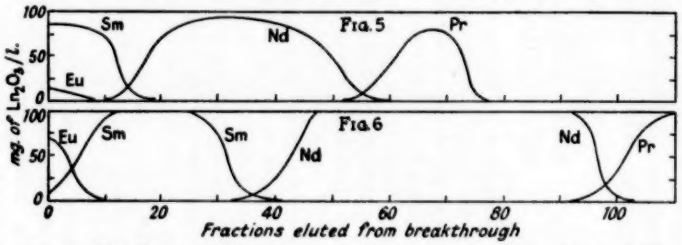


FIG. 5. *Enta* (5·2 × 10^{-3} *mol.*%), *eluant at* 750 *ml./hr.*

FIG. 6. *Enta* (5·2 × 10^{-3} *mol.*%), *eluant at* 1·5 *l./hr.*

apparent when it is realised that, in complex formation, acetic acid is monodentate, glycine is bidentate, citric acid tridentate, " trilo " quadridentate, and " enta " sexidentate. Concentrations of these eluants at 0·1% w/v represent molar concentrations of $1{\cdot}67 \times 10^{-2}$, $1{\cdot}3 \times 10^{-2}$, $5{\cdot}2 \times 10^{-3}$, $5{\cdot}23 \times 10^{-3}$, and $3{\cdot}4 \times 10^{-3}$%, respectively. The close similarity of the molar concentrations of citric acid and " trilo " obviated the necessity for further comparison of these eluants on a concentration basis. The higher molar concentrations of acetate and glycine coupled with their low efficiencies as eluants indicate that, in spite of the great influence of altered flow rate on their effectiveness in separation of the lanthanons, these eluants cannot compete with citrate on the basis of molar efficiency—at least, when Dowex-50 is the exchanging resin. The greatly enhanced separations obtained with " enta " at high flow rates at a lower molar concentration than citrate rendered necessary a further run for comparison of the two at similar molar concentrations. Figs. 5 and 6 show the elutions obtained with " enta " at $5{\cdot}2 \times 10^{-3}$ mol.% (*i.e.*, 0·152 w/v) at the citrate standard flow rate and 100% higher. The increase in efficiency shown by these elutions does not appear to confirm the generalisation by Spedding *et al.* (*loc. cit.*) that better separations are obtained with more dilute eluants. Instead, there appears to be a relation, not only between the stabilities of the complexes and flow rate as previously indicated, but also between the stabilities and eluant concentration effect when this latter is based on % w/v.

In elutions of the lanthanons from an Amberlite resin with " trilo," Fitch and Russell (*loc. cit.*) found that cadmium could be introduced into the exchanging system with a beneficial effect on the samarium–neodymium separation. This would suggest that the Cd–" trilo " complex has a stability intermediate between those of the Sm– and the Nd–" trilo " complex. However, Schwarzenbach and Freitag (*Helv. Chim. Acta*, 1951, **34**, 1942) found the overall stability constant (log $\overline{K}$) for " trilo " complexes with cadmium to be 9·54 compared with 10·37 for lanthanum, *i.e.*, the cadmium–" trilo " complex has a lower stability than has the lanthanum complex. The interpolation of cadmium between neodymium and samarium cannot be attributed to ionic sizes (0·97, 1·15, and 1·13 Å, respectively), so the reason for the difference between the elution series and the stability series is obscure unless the complexes formed in the resin column are different from those formed in the system studied by Schwarzenbach and Freitag. However, Fitch and Russell did not apparently consider the influence of molecular ratios when including cadmium in their elutions.

The log $\overline{K}$ values of lanthanon complexes with " enta " have recently been given by the author (*J.*, 1952, 1895); Schwarzenbach and Freitag (*loc. cit.*, p. 1503) have also reported the constants for several bivalent metal complexes with " enta." Consideration of these values, given in the table, shows two groups of interpolations: cobalt, zinc, and

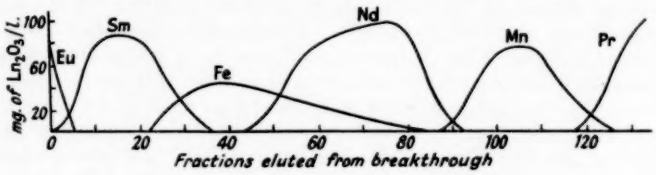
Overall stability constants for " enta " complexed ions.

Ion	log $\overline{K}$	Ion	log $\overline{K}$	Ion	log $\overline{K}$	Ion	log $\overline{K}$
Mn^{2+}	13·47	Zn^{2+}	16·15	Sm^{3+}	17·2	Pb^{2+}	18·2
Fe^{2+}	14·22	Cd^{2+}	16·48	Gd^{3+}	17·2	Cu^{2+}	18·38
La^{3+}	15·3	Pr^{3+}	16·55	Y^{3+}	18·0	Ni^{2+}	18·45
Ce^{3+}	16·05	Nd^{3+}	16·75	Er^{3+}	18·15	Yb^{3+}	18·70
Co^{2+}	16·1						

cadmium between cerium and praseodymium, and lead, copper, and nickel between erbium and ytterbium. The interpolation of copper at about the region of thulium is interesting because Marsh (*J.*, 1950, 1819) used cupric acetate in exchange separations of the lighter lanthanons but did not extend its use to separation of the heavier earths. It was understood, however, that copper salts would completely remove the lanthanons from an " enta " complex solution. This affords an example similar to that of Fitch and Russell, that overall stability constants of bivalent ions determined in acid–base titration systems appear to be somewhat increased when those bivalent ions are present in a predominantly tervalent-ion system. Confirmation of this was found in two further elutions with " enta," one of light, and the other of heavy lanthanons. Cobalt, zinc, and cadmium chlorides were added to the light lanthanon chloride solution, and copper and nickel chlorides to the heavy

lanthanon solution before adsorption and elution. Elutions were carried out with " enta " eluant at pH values of 6·8 and 4·2 respectively, with an " enta " concentration of $5{\cdot}2 \times 10^{-3}$ mol.% and a flow rate of 1250 ml./hour. The elution curves showed the Co–Zn–Cd interpolation to spread itself into the Sm–Eu–Gd region whilst the Cu–Ni interpolation disappeared altogether, the bivalent ions being completely eluted before the lanthanons. The direction of the displacement effect referred to above focused attention on manganese and iron. The " enta " complexes with these two metals are placed somewhat lower in the stability series than any of the lanthanons, and it was of interest to determine the degree to which complexes of these ions would be displaced on elution. An elution of light lanthanon chlorides with added ferrous and manganese chlorides was carried out, " enta " being used under the conditions given above. The elution curves obtained are shown in Fig. 7. The degree of separation of praseodymium and neodymium by manganese inter-

FIG. 7. *Interpolation of* Fe^{3+} *and* Mn^{2+} *ions in light lanthanon elutions with " enta."*



polation is striking; the elution of iron with, and before, neodymium is interesting and is ascribed to a certain extent to oxidation to the tervalent state during elution. Subsequent elutions employing manganese ions as the only addition to a 27% Pr_2O_3 + 72% Nd_2O_3 mixture yielded praseodymium of 98% purity and neodymium free from all traces of praseodymium determinable spectrophotometrically, with four intermediate fractions containing manganese and small quantities of lanthanons.

EXPERIMENTAL

The preliminary titrations were carried out with the lanthanons at a concentration of 5×10^{-3}M, and the carboxylic acids at 2×10^{-2}M. Nitric acid was added to give a strong acid concentration of 1×10^{-2}N, and the titrations were made with 1·25N-sodium hydroxide from a microburette. The change in pH was followed through a glass–calomel electrode system, a Marconi–Ekco pH meter being used.

The arrangement in these laboratories of the ion exchange assembly for lanthanon fractionation is briefly as follows: Six or more resin columns are set up in a tubular-steel scaffolding structure carrying, at 8 ft., a platform on which stand six or more 20-l. carboys. Eluant is prepared from demineralised water in a 100-gallon glass-lined vat beneath the carboy platform, and is pumped to each of the carboys *via* a manifold. The use of carboys on the platform instead of another tank is preferable, as it is then possible to keep, say, four columns operating on a standard eluant whilst other columns, fed from different carboys, are being used to evaluate different complexing agents as eluants. In the latter instances the eluant is prepared in a smaller tank at ground level and pumped to the appropriate carboy *via* the manifold.

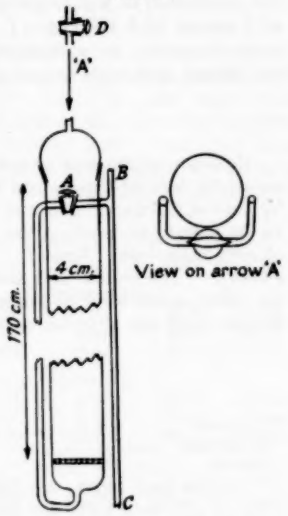
The construction of the resin columns shows some modification from that of previous workers and is shown diagrammatically in Fig. 8. After passage through the resin bed, the eluant has to rise to the stopcock *A*; this ensures that the resin bed is always covered with liquid, syphoning being avoided by the provision of an air port at *B*. Backwashing for removal of fines and air bubbles is accomplished by attachment of the water inflow to *C* and blocking *B* with a small rubber stopper. With the tap *D* fully open, the flow rate is controlled by tap *A*; when the flow rate has been correctly adjusted, tap *A* is no longer touched, any temporary cessation of operation being effected by closing *D*.

The resin employed for these studies was Dowex-50 of 30—50-mesh grain size. The resin was pretreated in the usual way, finishing in the acid form. For elutions with the resin in the ammonium form, the acid resin was given a final wash of 30 l. of 3% ammonia solution.

The lanthanon mixture generally employed was a combination of light lanthanons *ex* monazite (minus cerium) and heavy lanthanons *ex* yttrotitanite. Some yttrium had been

removed from these by ferricyanide fractionation. The light lanthanon mixture employed in later runs had been derived from monazite; cerium had been removed, and the remaining earths subjected to a series of fractional fusions with ammonium nitrate which removed much of the lanthanum at the head (Vickery, *J.*, 1949, 2508). Three tail fractions were combined to give the oxide mixture used here. Analyses of these original oxides and of the eluted fractions were made spectrophotometrically in a Beckman DU quartz spectrophotometer, Moeller and Brantley's extinction coefficients (*Anal. Chem.*, 1950, **22**, 433) being used. Yttrium contents were determined initially by difference and then confirmed by average atomic weight determinations. The two original oxides gave the following analyses. Light lanthanons: Pr_2O_3, 5·7; Nd_2O_3, 45·7; Sm_2O_3, 14·5; Eu_2O_3, 1·0; Gd_2O_3, 5%. Mixed lanthanons: Pr_2O_3, 9·5; Nd_2O_3, 20·6; Sm_2O_3, 10·2; Eu_2O_3, 1·5; Dy_2O_3, 6·2; Er_2O_3, 9·7; Yb_2O_3, 4·0%.

FIG. 8.



10-G. quantities of oxides were adsorbed on the resin beds from chloride solutions, and the beds then washed with the demineralised water until the runnings were free from chloride. Unless otherwise indicated in the figures, elution was carried out at a flow rate of 750 ml./hour, the eluate being collected in 5-l. fractions up to the breakthrough and thereafter in 750-ml. fractions. The lanthanons in the eluate were precipitated as oxalates, filtered off, ignited, weighed, and analysed as indicated above.

Separation of the lanthanons from the ions used as interpolants presented little difficulty in the dilute solutions involved, two oxalate precipitations being sufficient to remove all but traces of the alien metals. Determinations of iron, manganese, cobalt, etc., were carried out by the usual methods—generally ending gravimetrically—on the eluted solutions after removal of lanthanons with oxalic acid and evaporation to dryness to remove organic matter. Absolute accuracy in these determinations was not aimed at, it being sufficient to appreciate where the alien ions were eluted.

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836. *Dissociation Constants of the Alkaline-earth Salts of Some Monocarboxylic Acids.*

By C. A. COLMAN-PORTER and C. B. MONK.

The dissociation constants of a number of organic salts of calcium, strontium, and barium have been obtained from the solubilities of the iodates in solutions of the sodium salts of the acids. The results are discussed in terms of inductive effects, ion sizes, and ionisation potentials. Chelation occurs when the anion contains an OH or NH_2 group.

IN a previous paper (Lloyd, Wycherley, and Monk, *J.*, 1951, 1786) the dissociation constants of some cupric salts of organic acids were reported and the values compared with those of the corresponding acids. Inductive effects, which can largely account for the variations in the constants of the acids (Dippy, *Chem. Reviews*, 1939, **25**, 351), can also explain some of the trends in the cupric series. There are marked differences, however, since the cupric salts of hydroxy-acids show chelation, and the inductive effects appear to be modified by the size and charge of the cupric ion.

Owing to the lack of sufficient data for other salts it is not clear what influences can be attributed to the nature of the cation and we have therefore extended our studies to the

alkaline-earth series in the hope that these cations, whose properties vary systematically, will reveal further information. The solubility method used previously for the cupric salts (*loc. cit.*) was adopted. This method, which depends on the solubility of the iodate in solutions of the sodium salts of the acids, was first used by Davies (*J.*, 1938, 277) to study the ionisation of some calcium salts of organic acids. Apart from these results, and those of Cannan and Kibrick (*J. Amer. Chem. Soc.*, 1938, **60**, 2314) which are based on pH measurements, no systematic studies of the particular salts considered here have been published, although some isolated figures (to which reference is made later) are available.

Experimental

Calcium iodate was prepared by the method of Wise and Davies (*J.*, 1938, 273), barium iodate by that of Davies and Wyatt (*Trans. Faraday Soc.*, 1949, **45**, 770), and strontium iodate by that of Colman-Porter and Monk (*J.*, 1952, 1312). The solubility determinations were made as described previously (*idem, ibid.*). Solutions of the sodium salts were prepared by addition of carbonate-free " AnalaR " sodium hydroxide to solutions of the acids until the pH was about 7. The formic and acetic acids were " AnalaR," Kahlbaum's lactic acid was used, and the other acids were of laboratory grade except *iso*butyric acid, which was a triple-distilled sample, and the glycollic acid. This was prepared by hydrolysis of " AnalaR " chloroacetic

Table 1.

	Soly. in water (10^3M)	10^3{S.P.}	$K_{MIO_3^+}$	K_{MOH^+}
Calcium	7·84	71·19	0·13 [a]	0·05 [b]
Strontium	5·87	32·89	0·10 [c]	0·11 [c]
Barium	0·809	0·1480	0·08 [d]	—

[a] Wise and Davies, *loc. cit.* [b] Davies and Hoyle, *J.*, 1951, 233. [c] Colman-Porter and Monk, *loc. cit.* [d] MacDougall and Davies, *loc. cit.*

Table 2. *Solubility data obtained by using calcium iodate* (concns. $\times 10^3$).

[NaR]	Soly.	[CaR$^+$]	10^3I	K	[NaR]	Soly.	[CaR$^+$]	10^3I	K
		Formate					*n*-Valerate		
51·10	9·67	0·96	77·1	0·17	33·69	9·03	0·22	59·3	0·54
61·00	9·96	1·24	87·2	0·15	43·24	9·28	0 31	69·3	0·48
75·00	10·25	1·35	101·8	0·17	53·34	9·52	0·38	80·0	0·47
		Acetate					*iso*Valerate		
37·27	9·27	0·71	62·6	0·18	32·82	9·15	0·20	64·8	0·68
51·00	9·68	0·99	76·9	0·16	55·96	9·55	0·30	82·8	0·63
72·13	10·21	1·39	98·8	0·16	62·46	9·69	0·36	89·6	0·57
		Propionate					Trimethylacetate		
46·71	9·47	0·66	72·7	0·23	28·52	8·93	0·32	53·6	0·32
59·88	9·83	0·93	86·3	0·20	43·28	9·36	0·54	69·2	0·27
75·00	10·19	1·18	102·0	0·19	62·69	9·83	0·77	89·5	0·26
		n-Butyrate					Bromoacetate		
57·73	9·70	0·66	84·3	0·28	50·03	9·47	0·43	76·5	0·39
68·22	9·91	0·71	95·3	0·31	60·00	9·71	0·56	86·8	0·35
78·72	10·16	0·90	106·2	0·27	72·99	9·95	0·56	100·5	0·42
		*iso*Butyrate					Glycine salt [a]		
32·63	9·04	0·36	58·0	0·32	35·40	9·74	2·05	59·2	0·046
43·99	9·35	0·48	70·0	0·31	51·43	10·41	2·92	75·6	0·045
74·32	10·05	0·80	101·6	0·29	66·34	10·98	3·59	90·8	0·044

[a] The glycine solutions were made from equal concentrations of HR and NaOH. They were corrected for hydrolysis: pH = 11·3, 11·0, 11·0; [OH$^-$] = 2·48, 1·25, 1·29 ($\times 10^3$); [Ca(OH)$^+$] = 0·15, 0·07, 0·07 ($\times 10^3$), respectively.

acid with marble chips; the resulting calcium glycollate was recrystallised from water until it was chloride-free, and then converted into the acid by a column of the ion-exchange resin Amberlite I.R.-100.

The calculations were made as in previous cases (Davies, 1938, *loc. cit.*; Lloyd, Wycherley, and Monk, *loc. cit.*). Representing the cations by M^{2+} and the organic anions by R^-, we have

$$\log [M^{2+}][IO_3^-]^2 - 3F(I) = \log \{S.P.\}$$

where {S.P.} represents the solubility product and

$$F(I) = \log\{I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}2I\} \quad \text{(Davies, } J.\text{, 1938, 2093)}$$
$$[MR^+] = \text{Solubility} - [M^{2+}] - [MIO_3^+]$$
$$[R^-] = 2[M^{2+}] + [MIO^{3+}] + [Na^+] + [MR^+] - [IO_3^-]$$
$$\log K = \log [M^{2+}][R^-]/[MR^+] - 2F(I)$$

Allowance was made for undissociated sodium iodate (MacDougall and Davies, *J.*, 1935, 1416), for which $K = 3{\cdot}0$ and for the ion-pairs formed between M^{2+} and IO_3^- (the dissociation constants of these are given in Table 1). Since the glycine and alanine solutions were alkaline, pH measurements of these were made to correct for OH^- and $M(OH)^+$ ions. Table 1 contains the dissociation constants of the latter, together with the solubilities of the iodates in water at 25° ±0·03°. The concentrations and results of the calculations are summarised in Tables 2—4.

TABLE 3. *Solubility data obtained by using strontium iodate* (concns. $\times 10^3$).

[NaR]	Soly.	[SrR$^+$]	10^3I	K	[NaR]	Soly.	[SrR$^+$]	10^3I	K
		Formate					Bromoacetate		
44·55	7·21	0·56	64·2	0·21	50·03	7·20	0·25	70·3	0·53
66·82	7·61	0·68	87·4	0·24	60·00	7·37	0·30	80·6	0·52
75·47	7·78	0·83	96·2	0·22	72·99	7·58	0·34	94·1	0·54
		Acetate					Glycollate		
33·75	6·90	0·26	53·1	0·36	46·68	7·71	1·87	65·2	0·055
50·93	7·26	0·38	71·1	0·35	56·95	8·10	2·42	75·5	0·048
67·50	7·55	0·47	88·3	0·36	75·00	8·50	2·75	94·1	0·053
		Propionate					Lactate		
52·63	7·24	0·23	73·0	0·61	19·96	6·66	0·50	38·2	0·110
70·41	7·54	0·32	91·4	0·56	39·92	7·27	0·97	59·5	0·105
77·84	7·65	0·34	99·2	0·58	59·88	7·72	1·24	79·6	0·112
		n-Butyrate					Glycine salt *		
50·10	7·19	0·19	70·4	0·71	39·00	7·20	0·82	58·1	0·119
61·48	7·38	0·24	82·2	0·67	47·04	7·37	0·88	66·5	0·128
77·39	7·61	0·27	98·6	0·73	70·64	7·89	1·28	90·8	0·123
		n-Valerate					Alanine salt *		
57·82	7·28	0·10	78·5	1·5	40·12	7·13	0·57	59·5	0·180
70·40	7·48	0·13	91·7	1·4	58·76	7·52	0·76	78·9	0·187
		Trimethylacetate			70·92	7·75	0·89	91·4	0·186
48·59	7·15	0·17	68·8	0·70					
62·79	7·40	0·23	83·6	0·71					
73·94	7·57	0·35	95·2	0·75					

* The glycine and alanine solutions were made from equal concentrations of acid and sodium hydroxide. They were corrected for hydrolysis: (*a*) Glycine: pH = 10·6, 11·1, 11·1; $[OH]^- = 0{\cdot}60$, 1·60, 1·60 ($\times 10^3$); $[Sr(OH)^+] = 0{\cdot}02$, 0·04, 0·03 ($\times 10^3$), respectively. (*b*) Alanine: pH = 10·8, 10·9, 11·0; $[OH^-] = 0{\cdot}80$, 1·00, 1·30 ($\times 10^3$); $[Sr(OH^+)] = 0{\cdot}02$, 0·02, 0·03 ($\times 10^3$), respectively.

TABLE 4. *Solubility data obtained by using barium iodate* (concns. $\times 10^3$).

[NaR]	Soly.	[BaR$^+$]	10^3I	K	[NaR]	Soly.	[BaR$^+$]	10^3I	K
		Formate					*n*-Valerate		
51·10	1·130	0·088	54·3	0·26	57·82	1·125	0·015	61·1	1·8
61·00	1·171	0·115	64·2	0·23	70·40	1·162	0·022	73·8	1·4
75·00	1·213	0·128	78·3	0·25					
		Acetate					Trimethylacetate		
37·27	1·070	0·051	40·3	0·35	62·79	1·146	0·035	66·1	0·82
51·00	1·120	0·054	54·2	0·44	70·40	1·177	0·038	77·4	0·86
72·13	1·191	0·082	75·5	0·38					
		Propionate					Glycollate		
59·88	1·141	0·038	63·2	0·72	36·45	1·112	0·179	39·4	0·090
74·94	1·182	0·045	78·3	0·73	56·95	1·209	0·251	60·0	0·092
88·30	1·217	0·054	91·7	0·70					
		n-Butyrate					Lactate		
52·30	1·111	0·024	55·5	1·0	19·96	0·997	0·065	22·8	0·15
59·59	1·135	0·028	62·9	1·0	39·92	1·096	0·096	43·0	0·19
77·39	1·184	0·034	80·8	1·0	59·88	1·184	0·162	63·1	0·16

Discussion

The average dissociation constants, together with those collected from other sources, are given in Table 5. The values for magnesium acetate, propionate, butyrate, lactate, and glycollate were calculated from Cannan and Kibrick's data (*loc. cit.*). The original figures are not comparable with ours since they are based on measurements made at an ionic strength of 0·2 by an E.M.F. method of a somewhat empirical nature. The differences between the pK data of their calcium and magnesium results were used to estimate the values for magnesium salts given in Table 5 from our calcium results.

Table 5.—*Average dissociation constants at 25°.*

Anion	Mg	Ca	Sr	Ba	Limiting anion mobility
(1) Formate	—	0·16	0·22	0·25	54·6 [g]
(2) Acetate	0·165 [a]	0·17	0·36	0·39	40·9 [g]
(3) Propionate	0·19 [a]	0·21	0·58	0·71	35·8 [g]
(4) *n*-Butyrate	0·275 [a]	0·29	0·70	1·0	35·1 [h]
(5) *iso*Butyrate	—	0·31	—	—	34·2 [h]
(6) *n*-Valerate	—	0·50	1·5	1·6	33·4 [h]
(7) *iso*Valerate	—	0·63	—	—	32·7 [h]
(8) Trimethylacetate	—	0·28	0·72	0·84	31·9 [h]
(9) Bromoacetate	—	0·39	0·53	0·57 [c]	39·3 [i]
(10) Lactate	0·047 [a]	0·034 [c]	0·109	0·17	—
(11) Glycollate	0·039 [a]	0·026 [c]	0·049	0·091	—
(12) Glycine salt	0·0085 [b]	0·045	0·123	0·17 [f]	—
(13) Alanine salt	0·016 [b]	0·058 [d]	0·184	0·17 [f]	—

[a] Cannan and Kibrick (corrected). [b] Monk, *Trans. Faraday Soc.*, 1951, **47**, 297. [c] Davies, *loc. cit.* [d] Davies and Waind, *J.*, 1950, 301. [e] Davies and Wyatt, *loc. cit.* [f] Monk, *Trans. Faraday Soc.*, 1951, **47**, 1233. [g] Harned and Owen, "Physical Chemistry of Electrolytic Solutions," Reinhold, 1943, p. 172. [h] Dippy, *J.*, 1938, 1222. [i] I.C.T., VI, 262.

There are very few published data with which comparisons can be made. Davies and Wyatt (*loc. cit.*) cite a lower figure of 0·28 for calcium bromoacetate, but this was based on a personal communication and it is not possible to account for the difference. Bell and Waind (*J.*, 1951, 2357) suggest that calcium acetate has a K of >2 on the basis of kinetic studies. This and other values given by these authors are higher than those obtained by other methods and they have intimated that the kinetic values may be subject to error. Two series of results have been published for the calcium glycine salt. Davies (*loc. cit.*) quotes 0·045 and 0·038 from two measurements, and Davies and Waind (*loc. cit.*) obtained 0·037. Our measurements clearly support Davies's higher value. Joseph (*J. Biol. Chem.*, 1946, **164**, 529) studied a number of organic salts by an E.M.F. method, but calculated the apparent dissociation constants at an ionic strength of 0·15. Applying an approximate correction for this, we have $K = 0{\cdot}10$ for calcium acetate and 0·048 for calcium lactate. These are of the same order as the results given in Table 5, but differ numerically.

The dissociation constants of the salts of organic acids are undoubtedly related to the characteristics both of the cations and of the organic anions. First, it is apparent that our K values are in the order Ba > Sr > Ca > Mg. The lactate and glycollate of magnesium are possible exceptions but, for the reasons mentioned earlier, they may not be the true values. The general order is in the reverse direction to that found when these cations associate with low-valency inorganic anions, for which it has been suggested that hydrated ions form the ion pairs (Jones, Monk, and Davies, *J.*, 1949, 2693; Denney and Monk, *Trans. Faraday Soc.*, 1951, **47**, 992). A first suggestion with the organic series is therefore that association may involve unhydrated cations, since the crystallographic radii of the alkaline-earth cations (Table 6) have the same trend as the dissociation constants of the organic salts. This cannot be completely true, however, since the differences in the K values are not so marked as are the differences between the cation radii and furthermore would not account for the much smaller values of the cupric salts (*loc. cit.*). One possibility to account for the stability of metallic complexes formed with chelating agents such as aldehydes and amines is that their stabilities may be related to the ionisation potentials of the metals (Irving and Williams, *Nature*, 1948, **162**, 746; Calvin and Melchior, *J. Amer. Chem. Soc.*, 1948, **70**, 3270). This has so far only been applied to the transition metals and

where chelation occurs. We have applied this concept to our own data in a few cases, and Fig. 1 shows a plot of some pK values against the second ionisation potentials of the alkaline-earth metals and copper (Table 6; data of Ahrens, *Nature*, 1952, **169**, 463; Rice,

TABLE 6.

	Mg	Ca	Sr	Ba	Cu
Second ionisation potentials (ev)	15·03	11·82	10·98	9·95	20·3
Ionic radii (Å)	0·66	1·18	1·32	1·53	0·72

"Electronic Structure and Chemical Binding," McGraw-Hill, New York, 1940, pp. 98, 220). The results do not cover enough metals for a thorough discussion, but the plots do indicate that there is a rough relation. Similar plots are obtained with the other anions.

With these organic anions, the electrical centre is located at the carboxyl group, and is subject to a certain amount of displacement which is due partly to interionic forces and

FIG. 1.

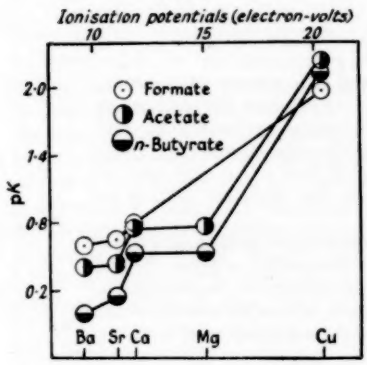
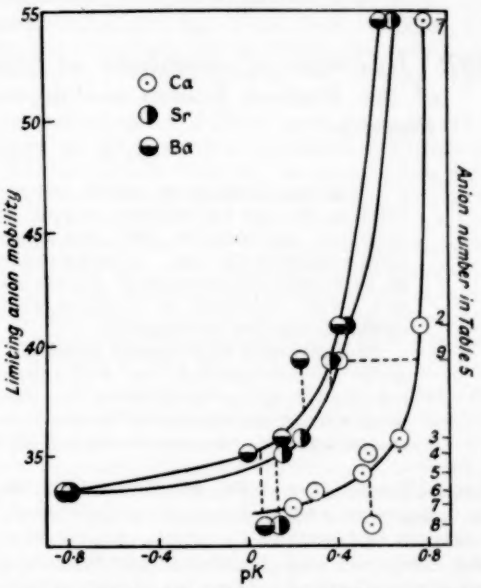


FIG. 2.



partly to the inductive effects of the various groups attached to the carboxyl group. Such displacements probably do not occur to any marked extent with inorganic anions owing to their electrical symmetry. The effects of electron-displacing groups on the dissociation constants of acids (Dippy, *loc. cit.*) were found to be considerably modified on replacing hydrogen by cupric ions (*loc. cit.*), and it is apparent that with the alkaline-earth cations inductive effects have little influence on the extent of ionisation. The main effects of the anions appear to depend on their relative sizes, which are no doubt related to the influence of the attached groups on the mean statistical distances of closest approach of the electrical centres of the associating ions. Plots illustrating this point are shown in Fig. 2, where the pK data are plotted against the limiting anion mobilities (Table 5). The latter, from Stokes's law, are related to the mean anion radii. The only cases where inductive effects appear to modify the effective anion size are the trimethylacetates and bromoacetates.

Where hydroxyl and amino-groups are present, the dissociation constants of the salts are much smaller. It has been previously remarked in conjunction with calcium salts (Davies, *loc. cit.*) that this can be attributed to chelation; the cupric salts (*loc. cit.*) and the present data conform to this view. Introduction of a methyl group markedly decreases the dissociation constants of the salts of these two types of acid. Although these differences may be due to the increase in the mean anion radius, yet this increase may not be sufficient

to account for all of the marked changes on passing from glycollate to lactate, and from the glycine to the alanine salt. Thus the limiting anion mobilities of the former pair are 40·8 and 35·5 respectively (unpublished work), indicating a radius ratio of 1 : 1·15, while the dissociation constant ratios vary from 1·3 to 2·0. It would appear that the methyl group modifies the binding capacity of the chelating group.

It seems then, from the available evidence, that the dissociation constants of the monocarboxylate salts become smaller (*a*) with metals of higher ionisation potentials and (*b*) if chelating groups are present in the anion, and increase as the anion size increases. Induction effects, which are short-range forces, become of less importance with metals of low ionisation potential. There are still, however, the effects of cation size and ion-solvation to consider, but until other metals, especially magnesium (which is the most hydrated alkaline-earth cation) have been investigated, these aspects remain obscure.

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837. *Hydrolysis of Substituted* o-*Chlorobenzoic Acids. The Mechanism of the Reaction between* o-*Halogenobenzoic Acids and Nucleophilic Reagents.*

By A. A. GOLDBERG.

2-Chloro-4-nitrobenzoic acid is not hydrolysed in presence of a copper catalyst by aqueous sodium acetate, disodium hydrogen phosphate, or potassium carbonate at 100°, but aqueous potassium carbonate at 150° gives 4-nitrosalicylic acid. Aqueous potassium hydroxide affords high yields of 3 : 3′-dichloroazobenzene-4 : 4′-dicarboxylic acid but no 4-nitrosalicylic acid. The hydrolysis of *o*-chlorobenzoic acids by aqueous potassium carbonate appears to be general.

It is suggested that reaction between *o*-halogenobenzoic acids and nucleophilic reagents proceeds *via* a non-ionised six-membered copper chelate complex (II) and is mediated by two independent electronic displacements, so that it can only proceed in an environment which allows formation of the chelate complex. Support is adduced for this view from other reactions.

SINCE Ullmann (*Ber.*, 1903, **36**, 2383; 1904, **37**, 853) discovered the high reactivity of the halogen in *o*-halogenobenzoic acids towards aniline and phenol in the presence of potassium carbonate and a copper catalyst many substituted *o*-chlorobenzoic acids have been condensed with arylamines and phenols, giving various 2-carboxy-diphenylamines and -diphenyl ethers. These are important because of their convertibility into acridones and xanthones respectively. Other nucleophilic reagents such as ammonia, alkylamines, and alcohols have been successfully condensed with *o*-chlorobenzoic acids but little has been recorded on the reaction of *o*-chlorobenzoic acids with water, *i.e.*, their hydrolysis into simple salicylic acids. The present work had its origin in a search for an easy route to 4-nitrosalicylic acid which was required for the preparation of 4-aminosalicylic acid.

Ullmann (*Annalen*, 1907, **355**, 360) failed to obtain 4-nitrosalicylic acid by the action of aqueous sodium hydroxide on 2-chloro-4-nitrobenzoic acid but succeeded in effecting the hydrolysis with lime-water at 150°; the method has, however, experimental disadvantages (cf. Wenis and Gardner, *J. Amer. Pharm. Assoc.*, 1950, **38**, 9). Since salicylic acid is obtainable by the hydrolysis of *o*-bromobenzoic acid with aqueous sodium acetate (Hurtley, *J.*, 1929, 1870) it was thought desirable to examine the reaction, in the presence of a copper catalyst, of 2-chloro-4-nitrobenzoic acid with aqueous solutions of various inorganic acid-acceptors of increasing basic strength. Those selected were sodium acetate, disodium hydrogen phosphate, potassium carbonate, and potassium hydroxide. Aqueous sodium acetate, disodium hydrogen phosphate, and potassium carbonate at 100° for periods as long as 24 hours were without action. At 150°, however, aqueous potassium carbonate gave almost quantitative yields of 4-nitrosalicylic acid. The reaction appears to be generally applicable, since 2-chloro-3- and 2-chloro-5-nitrobenzoic acid yielded

respectively 3- and 5-nitrosalicylic acid, and 2 : 3-, 2 : 4-, and 2 : 5-dichlorobenzoic acids gave 3-, 4-, and 5-chlorosalicylic acid, all in high yield. Attempts to effect the hydrolysis without the use of pressure were less successful; concentrated aqueous potassium carbonate in refluxing amyl alcohol was without action; potassium carbonate in molten sodium acetate trihydrate at 130° gave only a poor yield.

With 10N-aqueous potassium hydroxide in amyl alcohol, at temperatures ranging from 95° to the reflux point (*ca.* 120°), 2-chloro-4-nitrobenzoic acid gave an almost theoretical yield of 3 : 3′-dichloroazobenzene-4 : 4′-dicarboxylic acid; no 4-nitrosalicylic acid was formed. The hydrogen necessary for the reduction of the nitro- to the azo-group apparently originates from the amyl alcohol but that this is not the entire explanation is shown by the production of the same compound, although in much smaller yield, by the action of aqueous potassium hydroxide in the absence of amyl alcohol [compare the reduction of *p*-chloronitrobenzene by sodium ethoxide in ethyl alcohol (Raiford and Colbert, *J. Amer. Chem. Soc.*, 1926, **48**, 2652) and the conversion of *m*-chloronitrobenzene by sodium methoxide into 3 : 3′-dichloroazoxybenzene (Hollemann, *Rec. Trav. chim.*, 1915, **35**, 1)]. The constitution of the dicarboxylic acid was determined by hydrogenation which, by reduction of the azo-group and simultaneous hydrogenolysis of the halogen, gave *p*-aminobenzoic acid.

The remarkable stability of the halogen substituent in 2-chloro-4-nitrobenzoic acid in the presence of the high hydroxyl-ion concentration of aqueous potassium hydroxide led to speculation on the mechanism of the general reaction between *o*-halogenobenzoic acids and anionoid reagents such as ammonia, amines, phenols, alcohols, and water, leading to ejection of the chlorine as chloride ion and its substitution by the fragment of the anionoid reagent. Ullmann (*Annalen*, 1907, **355**, 312) showed that the reaction proceeds smoothly only in the presence of traces of copper or its salts; iron, zinc, nickel, and platinum are also effective, but manganese and tin are inactive. Halogen substituents *para* to the carboxyl group do not react; for example, 2 : 4-dichlorobenzoic acid and the strongly nucleophilic *p*-anisidine give 90% yields of 2-carboxy-5-chloro-4′-methoxydiphenylamine (B.P. 353,537; Magidson *et al.*, *Chem. Pharm. Ind. U.S.S.R.*, 1935, **1**, 26; Magidson and Grigorski, *Ber.*, 1936, **69**, 396) [cf. 2 : 4-dichlorobenzoic acid with (*a*) aqueous ammonia (G.P. 244,207), (*b*) phenol (Ullmann, *Ber.*, 1904, **37**, 853), and (*c*) aqueous potassium carbonate (see below)].

The contrast between the reactivities of halogens in *o*- and *p*-halogenobenzoic acids, and the similarity of the reactivities of halogens in *o*- and *p*-halogenonitrobenzenes, is striking. It is significant that the copper catalyst, essential for the reaction between anionoid reagents and *o*-halogenobenzoic acids, is unnecessary for the reaction between the former and *o*- and *p*-halogenonitrobenzenes.

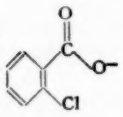
It appears that the effective initial catalyst in the reaction is a cuprous ion since cuprous iodide is an active catalyst in the presence of potassium iodide—environmental conditions under which cupric ion cannot exist (I. Goldberg, *Ber.*, 1907, **40**, 4541). Bunnett and Zahler (*Chem. Reviews*, 1951, **49**, 273) represent the catalyst as a cuprous ion which co-ordinates with the halogen, thus incipiently converting the latter into the 'onium state and increasing its replaceability in the same way as the lability of a substituted amino-group is increased by conversion into the quaternised condition (Königs and Greiner, *Ber.*, 1931, **64**, 1049; Borrows, Clayton, and Hems, *J.*, 1949, S 199); and the lability of iodine is increased by conversion into the iodonium state (Sandin *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 1550). This mechanism, however, gives no consideration to the obviously important role of the adjacent carboxyl group and the question of the functional state in which the latter group exists; nor does Bunnett and Zahler's suggestion explain the stability of halogen atoms *para* to the carboxyl group or the stability of *ortho*-halogen atoms towards potassium hydroxide.

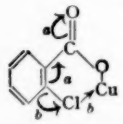
The reaction between *o*-chlorobenzoic acids and an arylamine apparently requires the presence of a small amount of water (Goldberg and Kelly, *J.*, 1946, 102), which is normally supplied by the neutralisation of the potassium carbonate by the *o*-chlorobenzoic acid and the hydrogen chloride eliminated during the reaction. The more strongly anionoid the arylamine, the lower is the temperature at which condensation takes place. Thus, aniline requires temperatures of *ca.* 130°, and *p*-toluidine and *p*-anisidine condense readily at

100—106°; *p*-dimethylaminoaniline gives high yields at 80° (Goldberg and Kelly, *loc. cit.*); *p*-aminophenol and 2 : 4-dichlorobenzoic acid at 60° give 50% yields of 2-carboxy-5-chloro-4'-hydroxydiphenylamine (personal communication from Mr. Besly). On the other hand the weakly anionoid *p*-nitroaniline condenses with difficulty, yields of only *ca.* 18% being obtained at 180° (Albert and Linnell, *J.*, 1936, 1614).

Although the condensation of an *o*-halogenobenzoic acid and a nucleophilic reagent is carried out in presence of excess of potassium carbonate it is most improbable that the reaction proceeds *via* the ion (I) since the carboxyl ion would induce electron-accession to $C_{(2)}$ of the benzene ring, thereby inhibiting attack by anionoid reagents at this point [cf. the chlorination of aqueous sodium benzoate which gives principally *o*-chlorobenzoic acid (Saint Evre, *Ann. Chim.*, 1849, **25**, 485; Lossen, G.P. 146,174); also the effect of the first carboxyl *ion* on the dissociation constant of the second carboxyl group in the benzenedicarboxylic acids (Robinson, *J.*, 1947, 1290)]. In addition, it has been shown (see below) that the *o*-halogen substituent is completely stable in the presence of aqueous potassium hydroxide, conditions under which it would be expected that the whole of the *o*-chlorobenzoic acid would exist as the ion (I).

It is now suggested that the reaction proceeds *via* a non-ionised six-membered chelate copper complex (II) and is mediated by two independent mechanisms: (*a*) the electromeric polarisation of the system C=C—C=O, and (*b*) the polarisation of the system C—Cl→Cu in which the normal inductive effect in the C↔Cl bond, and the inductometric polarisability of the bond in the presence of an attacking anionoid reagent, will be strongly augmented by the co-ordination of the chlorine with the copper. Both these processes operate in concert to create electron-defect on $C_{(2)}$ of the benzene ring, the combined total defect being sufficient to render this position easily susceptible to attack by nucleophilic reagents with consequent ejection of the chlorine as chloride ion. The polarisation (*a*) will be transmitted through the benzene ring, appearing as an electron defect at position 4; but this effect will be antagonised by, or at least not supported by, any transmission through the benzene ring of the "co-ordination polarisation" (*b*) which could only manifest itself as an electron-deficiency at position 3 or 5. The net electron-defect at position 4 will therefore be too small to initiate attack by nucleophilic reagents and accordingly halogen atoms at this position will be stable.

(I) 

 (II)

It would follow that environmental conditions which inhibit or suppress the Cl→Cu co-ordination bond or the O—Cu salt bond should restrain the course of the reaction. Determining conditions would be expected to be associated with the solvation and the basic strength of the acid acceptor employed. For example, potassium hydroxide is, potassium carbonate is not, soluble in amyl alcohol; accordingly it would be expected that suspensions of the latter in amyl alcohol would have no influence on the chelate complex (II) while solutions of potassium hydroxide in amyl alcohol would disrupt the C→Cl and the O—Cu bond. In addition it would be expected that excessive quantities of potassium carbonate, especially in the presence of water, would have some disruptive effect on the chelate heterocyclic system. It was therefore of interest to examine the reaction between *o*-chlorobenzoic acid and an arylamine of enhanced nucleophilic activity, *viz.*, *p*-toluidine, in amyl alcohol, with potassium carbonate and potassium hydroxide as acid acceptor. It was found that *o*-chlorobenzoic acid (1 mol.), *p*-toluidine (1·5 mols.), and potassium carbonate (2·5 equivs.) in amyl alcohol at 106° for 4 hours gave 4-carboxy-4-methyldiphenylamine in 85% yield. When the potassium carbonate was replaced by potassium hydroxide (2·5 equivs.) no reaction took place. In reactions carried out with potassium carbonate (2·5 equivs.) in amyl alcohol containing substantial amounts of water there was impairment of yield; the yield was further decreased by increasing the amount of the

carbonate (Table 1, p. 4373). Similar observations have been made regarding the action between 2 : 4-dichlorobenzoic acid and *p*-toluidine (Table 2, p. 4373).

Pertinent information is obtainable from the stability of the well-known chelate copper derivative of acetylacetone; the same underlying pattern is discernible. This substance is soluble in boiling amyl alcohol, giving a stable blue solution; on cooling, the complex crystallises unchanged. Addition of an equivalent of anhydrous or concentrated aqueous potassium carbonate effects no decomposition even on prolonged heating; excessive quantities of strong aqueous potassium carbonate effect slow decomposition; addition of one equivalent of potassium hydroxide causes immediate and complete disruption of the compound. Morgan and Drew (*J.*, 1920, 1456) record a similar stability pattern for the selenium derivative of acetylacetone.

Postulation of a chelate copper complex as the reaction intermediate is also supported by the familiar sequence of unusual and vivid colours which accompany reaction between *o*-halogenobenzoic acids and arylamines; production of striking colours is frequently diagnostic of metallic inner complex salts (Morgan and Drew, *loc. cit.*; Diehl, *Chem. Reviews*, 1937, **21**, 39).

Experimental

4-Nitrosalicylic Acid.—A solution of 2-chloro-4-nitrobenzoic acid (40·4 g., 0·2 mol.) in water (250 c.c.) and potassium carbonate (41·4 g., 0·6 equiv.) was heated with copper bronze (2 g.) and cuprous iodide (2 g.) in an autoclave at 145—150° (internal) and 75 lb./sq. in. for 8 hours without stirring. The brown liquid was diluted with boiling water, the small amount of yellow insoluble material filtered off, potassium chloride (40 g.) added, and the solution evaporated to *ca.* 300 c.c. and set aside to cool for several hours. The crystalline precipitate of potassium 4-nitrosalicylate was collected and dissolved in boiling water (100 c.c.), and the 4-nitrosalicylic acid (31·5 g.; m. p. 226—228°) precipitated by acidification to Congo-red with 10N-hydrochloric acid. Crystallisation from dilute alcohol gave the pure acid as pale yellow needles, m. p. 234° alone or mixed with a sample prepared from 4-nitroanthranilic acid (Found: equiv., 183; N, 7·8. Calc.: equiv., 183; N, 7·7%).

The yellow insoluble material, consisting of a copper complex salt of 4-nitrosalicylic acid and unchanged catalyst, was boiled with 2N-sodium hydroxide (30 c.c.) for ½ hour and the suspension filtered. Acidification of the filtrate precipitated a further 2·0 g. of pure 4-nitrosalicylic acid.

5-Nitrosalicylic Acid.—A solution of 2-chloro-5-nitrobenzoic acid (20·2 g.) in water (500 c.c.) and potassium carbonate (20·2 g.) was heated with copper bronze (1 g.) and cuprous iodide (1 g.) for 6 hours at 155—160° (pressure 70 lb./sq. in.). The filtered solution, treated as described above, yielded 5-nitrosalicylic acid (16·2 g.), m. p. 226—228°; crystallisation from very dilute alcohol gave the pure acid (13 g.) in long needles, m. p. 234° alone or mixed with authentic material (Found: equiv., 184; N, 7·6%).

3-Nitrosalicylic Acid.—A solution of 2-chloro-3-nitrobenzoic acid (10·1 g.) in water (250 c.c.) and potassium carbonate (10·4 g.) was heated with copper bronze (0·5 g.) and cuprous iodide (0·5 g.) for 6 hours at 160°. The filtered solution was evaporated to *ca.* 170 c.c. and chilled. The yellow needles of the potassium salt were collected and dissolved in boiling water (150 c.c.), and the solution acidified to pH 2 with hydrochloric acid and kept in the refrigerator overnight. The 3-nitrosalicylic acid was collected and dried; the yield was 6·1 g., and the m. p. 146—148° alone or mixed with authentic material (Found: equiv., 184; N, 7·5%).

4-Chlorosalicylic Acid.—A solution of 2 : 4-dichlorobenzoic acid (19·1 g.) in water (500 c.c.) and potassium carbonate (20·7 g.) was heated with copper bronze (1 g.) and copper iodide (1 g.) for 12 hours at 175—180° (130 lb./sq. in.). The filtered (charcoal) solution was chilled and acidified with 10N-hydrochloric acid to pH 2, and the precipitate collected; crystallisation from 50% alcohol (280 c.c.) yielded 4-chlorosalicylic acid in long colourless needles (11·1 g.), m. p. 216—218° alone or mixed with an authentic sample (Found: equiv., 173; Cl, 20·6%. Calc.: equiv., 172·5; Cl, 20·5%).

3-Chlorosalicylic Acid.—2 : 3-Dichlorobenzoic acid (19·1 g.), treated as described for the 2 : 4-isomer, yielded 3-chlorosalicylic acid (12·3 g.), m. p. 176—178° alone or mixed with authentic material (Found, in recrystallised material, m. p. 180°: equiv., 174; Cl, 20·6%).

5-Chlorosalicylic Acid.—A solution of 2 : 5-dichlorobenzoic acid (19·1 g., 0·1 mol.) in water (500 c.c.) and potassium carbonate (20·7 g., 0·3 equiv.) was heated with copper bronze (1 g.) and cuprous iodide (1 g.) for 12 hours at 160—170°/90 lb./sq. in. The resulting filtered solution

on acidification yielded 5-chlorosalicylic acid (14·8 g.), m. p. 170°; crystallisation from dilute methanol gave the pure acid in colourless needles, m. p. 172—174° (Found: equiv., 172; Cl, 20·6%).

4-*Nitrosalicylic Acid.*—2-Chloro-4-nitrobenzoic acid (20·2 g., 0·1 mol.) and anhydrous potassium carbonate (20·7 g., 0·3 equiv.) were added to molten sodium acetate trihydrate (250 g.) containing copper bronze (2 g.) and cuprous iodide (2 g.) and the mixture heated to 128—135° (internal) for 8 hours; water was allowed to distil away. Boiling water (200 c.c.) was added, the solid broken up, and the suspension filtered. The solid was boiled with N-potassium hydroxide (300 c.c.) for ½ hour, the insoluble material removed, and the filtrate acidified with hydrochloric acid. Purification *via* the potassium salt gave pure 4-nitrosalicylic acid (10·2 g.), m. p. 230—232° (Found: equiv., 184; N, 7·8. Calc.: equiv., 183; N, 7·7%).

Reaction of 2-*Chloro-4-nitrobenzoic acid with Aqueous-amyl-alcoholic Potassium Hydroxide:* 3 : 3′-*Dichloroazobenzene-4* : 4′-*dicarboxylic Acid.*—(a) *Reaction at* 90—95°. A solution of 2-chloro-4-nitrobenzoic acid (80·4 g., 0·4 mol.) in amyl alcohol (600 c.c.) and 10N-potassium hydroxide (100 c.c., 1 mol.) was stirred with copper bronze (5 g.) and cuprous iodide (5 g.) on the water-bath for 12 hours (internal temp. 90—95°). The amyl alcohol was distilled off in steam, the aqueous solution filtered and acidified with 5N-sulphuric acid, and the dark brown precipitate collected. This was drained and extracted for 1 hour with boiling 90% alcohol (800 c.c.) in which 2-chloro-4-nitrobenzoic and 4-nitrosalicylic acid are very soluble; the insoluble residue was a light brown powder (78 g.), m. p. >320°. This was dissolved in water and potassium carbonate monohydrate (234 g.), and the solution evaporated to small volume on the water-bath and chilled; the precipitated potassium salt (100 g.) was collected and dissolved in boiling water (300 c.c.), and the solution run into an excess of 2N-sulphuric acid stirred at 80°. The precipitate of the free acid (46 g.) was collected, washed with boiling water, and dried (Found: N, 8·1; Cl, 19·5%). It was too insoluble for purification by ordinary crystallisation but the following method of "slow precipitation-crystallisation" was effective. A solution of the acid (46 g.) in boiling water (400 c.c.) and pyridine (125 c.c.) was stirred at the b. p. and hot 5N-sulphuric acid added dropwise very slowly until the pH value was 4·0. 3 : 3′-*Dichloroazobenzene-4* : 4′-*dicarboxylic acid* separated as a cream-coloured microcrystalline powder (27 g.), m. p. 356° (Found: equiv., 171; C, 49·2; H, 2·2; N, 8·3; Cl, 20·7. $C_{14}H_8O_4N_2Cl_2$ requires equiv., 169·5; C, 49·5; H, 2·4; N, 8·3; Cl, 20·9%). Further acidification of the aqueous pyridine filtrate to pH 2·0 gave another 9 g. of the acid, m. p. 356° (Found: equiv., 170; N, 8·2; Cl, 20·6%).

(b) *Reaction at* 130°. 2-Chloro-4-nitrobenzoic acid (80·4 g., 0·4 mol.), amyl alcohol (500 c.c.), 10N-potassium hydroxide (100 c.c., 1 mol.), copper bronze (5 g.), and cuprous iodide (5 g.) were stirred together at the b. p. for 3 hours during which solvent (500 c.c.) was allowed to distil off, being replaced at regular intervals by a total of 400 c.c. of amyl alcohol. The mixture was then stirred at the b. p. for a further 4 hours. Isolation of the product as described above and extraction with boiling alcohol left 3 : 3′-dichloroazobenzene-4 : 4′-dicarboxylic acid (71 g.), m. p. >330°. Purification *via* the pyridine salt yielded pure acid (47 g.), m. p. 354°. A recrystallised sample had m. p. 356° (Found: equiv., 170·5; N, 8·4; Cl, 20·5%).

The following derivatives of 3 : 3′-dichloroazobenzene-4 : 4′-dicarboxylic acid were made: *acid chloride*, orange rosettes (from toluene), m. p. 120—122° (Found: N, 7·3; Cl, 37·4. $C_{14}H_6O_2N_2Cl_4$ requires N, 7·5; Cl, 37·8%); *ethyl* ester (from the chloride and alcohol), orange needles (from alcohol), m. p. 88° (Found: N, 7·3; Cl, 18·2. $C_{18}H_{16}O_4N_2Cl_2$ requires N, 7·1; Cl, 18·0%); *amide* (from the chloride and aqueous ammonia), orange needles (from pyridine–dioxan–water), m. p. 330° (Found: N, 16·5; Cl, 20·8. $C_{14}H_{10}O_2N_4Cl_2$ requires N, 16·6; Cl, 21·0%); p-*chloroanilide*, orange needles (from aqueous pyridine), m. p. 330—332° (Found: N, 9·9; Cl, 25·4. $C_{26}H_{16}O_2N_4Cl_4$ requires N, 10·0; Cl, 25·4%).

Hydrogenation of 3 : 3′-*Dichloroazobenzene-4* : 4′-*dicarboxylic Acid.*—The foregoing acid (3·4 g., 0·01 mol.) was dissolved in water (100 c.c.) and 2·5N-sodium hydroxide (15 c.c.), and 2·5N-acetic acid added until the pH was 8·3. 5N-Sodium hydroxide (5·0 c.c.) was added and the orange solution hydrogenated over Raney nickel at 20°/760 mm. Uptake of hydrogen was rapid (865 c.c. at N.T.P. in 2½ hours; no more after another 3 hours) (Calc. for reduction of azo- to amino-group with simultaneous dehalogenation: 896 c.c.). The catalyst was filtered off and washed with the filtrate; the colourless solution required 10·3 c.c. of 0·5N-sulphuric acid for adjustment to pH 8·3. Accordingly the amount of 5N-sodium hydroxide neutralised by the hydrogen chloride generated was 4·0 c.c. (Calc. for elimination of 2HCl per mol.: 4·0 c.c.). Dilute sulphuric acid was added until the pH was 4·0; the solution (250 c.c.), kept at 0° for 24 hours, deposited needles (1·4 g.) of *p*-aminobenzoic acid, m. p. 188—190° alone or mixed with

authentic material (Found: equiv., 137; N, 10·4. Calc.: equiv., 137; N, 10·2%). Electrometric analysis showed that the filtrate contained a total of 0·65 g. of chloride ion (Calc.: Cl^-, 0·71 g.).

Reactions between o-*Chloro- and* 2:4-*Dichloro-benzoic Acid and* p-*Toluidine with Potassium Carbonate or Potassium Hydroxide as Acid-acceptor.*—The method used is exemplified by the following. To *o*-chlorobenzoic acid (39·1 g., 0·25 mol.) in amyl alcohol (337 c.c.) potassium carbonate (43 g., 0·625 equiv.) was added during ½ hour, with stirring, at *ca.* 50°. Copper bronze (2 g.), cuprous iodide (2 g.), and *p*-toluidine (40·1 g., 0·375 mol.) were added and the mixture stirred at 104—106° (internal) for the stated time; no solvent was allowed to distil away. The amyl alcohol was removed in steam, the residual solution filtered, evaporated to a standard volume, and acidified with 5N-sulphuric acid to pH 4, and the 2-carboxy-4′-methyldiphenylamine filtered off. The filtrate was further evaporated and acidified to pH 2, then chilled, and the recovered *o*-chlorobenzoic acid collected. The aqueous filtrate was adjusted to a suitable volume and an aliquot analysed for chloride ion by electrometric titration with Ag/Pb–Hg electrodes. The 2-carboxy-4′-methyldiphenylamine and recovered *o*-chlorobenzoic acid were, when necessary, recrystallised until the m. p. was within 4° of the correct value and the identity of the products in all cases checked by mixed m. p.s and molecular-weight determination. For results see Tables.

TABLE 1. *Reaction between* o-*chlorobenzoic acid* (1 *mol.*) *and* p-*toluidine* (1·5 *mol.*) *at* 106°.

Acid-acceptor							
K_2CO_3 (equiv.)	KOH (equiv.)	Time (hours)	Amyl alcohol (c.c.)	Water (c.c.)	Cl^- liberated (g.-ion)	Yield [a] (mol.)	Recovered acid (mol.)
2·5	—	4	1350	—	1·04	0·85	—
2·5	—	8	1350	225	0·33	0·15	0·60
2·5	—	16	1350	225	0·48	0·35	0·55
2·5	—	24	1350	225	0·80	0·50	0·22
5·0	—	4	1350	—	0·99	0·72	—
5·0	—	4	1350	225	0·32	0·08	0·65
10·0	—	4	1350	—	0·15	0·05	0·70
10·0	—	4	1350	225	0·10	—	0·82
—	2·5	4	1350	—	0·02	—	0·92
—	2·5	16	1350	—	0·04	—	0·88
—	2·5	6	1350	225	0·02	—	0·87
—	2·5	16	1350	225	0·02	—	0·86

[a] 2-Carboxy-4-methyldiphenylamine.

TABLE 2. *Reaction between* 2:4-*dichlorobenzoic acid* (1 *mol.*) *and* p-*toluidine* (1·5 *mol.*) *at* 106°.

Acid-acceptor							
K_2CO_3 (equiv.)	KOH (equiv.)	Time (hours)	Amyl alcohol (c.c.)	Water (c.c.)	Cl^- liberated (g.-ion)	Yield [b] (mol.)	Recovered acid (mol.)
2·5	—	4	1350	—	1·02	0·94	—
—	2·5	4	1350	—	0·04	—	0·93
—	2·5	4	1350	225	—	—	0·96

[b] 2-Carboxy-5-chloro-4′-methyldiphenylamine.

Action of Potassium Carbonate and Potassium Hydroxide on the Copper Acetylacetone Salt.—(*a*) A solution of the copper derivative (1·0 g.) of acetylacetone in amyl alcohol (75 c.c.) was heated on the water-bath for 4 hours. On cooling, 0·84 g. of the complex separated in long blue needles. (*b*) A solution made as described above and heated with 2·5 c.c. of water and 0·7 g. of potassium carbonate on the water-bath for 4 hours gave a similar result. (*c*) A solution made as described above and heated with 10 c.c. of water and 2·5 g. of potassium carbonate for 4 hours on the water-bath gave a similar result. (*d*) Repetition of (*c*) with 6 g. of potassium carbonate gave 0·44 g. of recovered copper salt; the potassium carbonate layer was very dark brown. (*e*) To a solution of the copper salt (1·0 g.) in hot amyl alcohol (75 c.c.) was added potassium hydroxide (0·7 g.) in amyl alcohol (10 c.c.). The solution instantly became dark brown; on cooling, no copper salt separated.

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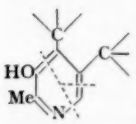
838. *Synthetical Experiments in the B Group of Vitamins. Part IV.* A Synthesis of Pyridoxine.*

By A. Cohen, J. W. Haworth, and E. G. Hughes.

Condensation of *N*-alkyl- or *N*-arylalkyl-alanine esters with α-formylsuccinic esters yields *N*-alkyl- or *N*-arylalkyl-*N*-1-carbalkoxyethylaminomethylenesuccinic esters (I). These are cyclised (Dieckmann) to basic keto-esters (II), the hydrochlorides of which yield pyridinium salts (IV) by dehydrogenation. The 1-benzylpyridinium salt (IV) gives, on hydrogenolysis, dialkyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylates which are convertible into pyridoxine by standard reactions (VI ⟶ X). Suitable quaternary ammonium bases convert 3-hydroxypyridines into their 3-ethers, *e.g.*, diethyl 3-benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R = Et, R′ = CH_2Ph) which during the reactions (VI ⟶ X) gives the 3-hydroxy-diamine (IX; R = H) by simultaneous hydrogenolysis and reduction of the nitrile groups in (VIII). By a shorter route, the 3-benzyloxy-diester is directly reduced by lithium aluminium hydride to pyridoxine benzyl ether which is hydrogenolysed to pyridoxine.

This communication presents details of a synthesis of pyridoxine which has been outlined elsewhere (cf. Festschrift E. C. Barrell, Basle, 1946, p. 71; XIth Internat. Congr. Pure and Appl. Chem., 1947, Abs. 247/3) and disclosed in patents (B.P. 551,216, 556,044, 591,170, 603,811, 625,997, 629,423, 629,450). Unlike syntheses based on an initial pyridone condensation (Harris, Folkers, and their co-workers, *J. Amer. Chem. Soc.*, 1939, **61**, 1245, 3307; Morii and Makino, *Enzymologia*, 1939, **7**, 385; Mowat, Pilgrim, and Carlson, *J. Amer. Chem. Soc.*, 1943, **65**, 954) or on oxidative degradation of an *iso*quinoline derivative (Kuhn, Westphal, Wendt, and Westphal, *Naturwiss.*, 1939, **27**, 469), the present synthesis was based on a hypothetical derivation of the B_6 group of vitamins from units of alanine, formaldehyde, and a four-carbon compound, as shown in the formula inset. This conception was independent of Snell and Guirard's evidence (*Proc. Nat. Acad. Sci.*, 1943, **29**, 66) that alanine was a micro-biological precursor of vitamin B_6. Subsequent work has shown that, although D-alanine, a common cell-constituent for many micro-organisms, can replace vitamin B_6 in culture media, it does not produce additional vitamin.

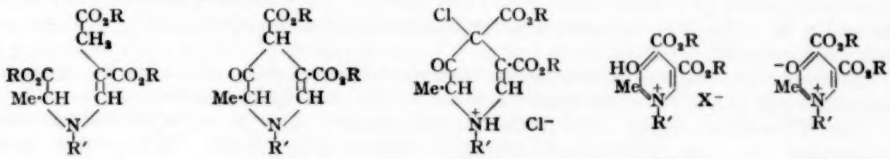


The reaction between DL-alanine ester and ethyl α-formylsuccinate was first studied as one of a number of analogous condensations (*J.*, 1950, 3005). The resulting *N*-substituted aminomethylenesuccinic ester (I; R = Et, R′ = H), like analogous compounds of this series, was found (*loc. cit.*) to yield, on cyclisation, not the desired cyclic keto-ester (cf. II) which was to be dehydrogenated to a 3-hydroxypyridine derivative, but a derivative of Δ^4-pyrrolin-2-one. It was realised that cyclisation to compounds of type (II) required an aminomethylenesuccinic ester completely substituted at the nitrogen atom, and therefore derived from a secondary α-amino-ester.

Accordingly, in a model synthesis, ethyl DL-α-methylaminopropionate was condensed with ethyl α-formylsuccinate, yielding ethyl *N*-1-carbethoxyethyl-*N*-methylaminomethylenesuccinate (I; R = Et, R′ = Me). This was cyclised by sodium, sodium ethoxide, or sodamide under the conditions of a Dieckmann reaction to the cyclic keto-ester (II; R = Et, R′ = Me). Although cyclisations to piperidones are well known and have often been reported since the initial conversion of bis-2-carbethoxyethylmethylamine into ethyl 3-keto-1-methylpiperidine-4-carboxylate by Prill and McElvain (*J. Amer. Chem. Soc.*, 1933, **55**, 1233), it is believed that this is the first instance of a Dieckmann cyclisation of aminomethylene compounds of type (I) to a dihydropyridone (cf. II). That such was the nature of the product was observable in the β-keto-ester character (ferric chloride reaction) and the formation, under anhydrous conditions, of a hydrochloride of a weak base, readily hydrolysed in water. Moreover, although simple

* Part III, Bergel, Hindley, Morrison, and Moss, *Chem. Ber.*, 1952, **85**, 711. Part II, *J.*, 1950, 3005.

dehydrogenation of the free base (II; R′ = Me) was not feasible, its hydrochloride was dehydrogenated when exposed to dry air or repeatedly recrystallised from alcohol–ether, yielding the pyridinium salt (IV). Dehydrogenation was more controllable when the keto-ester was treated with sulphuryl chloride: the primary oily product was readily converted when warmed under reduced pressure into crystalline 4 : 5-dicarbethoxy-3-hydroxy-1 : 2-dimethylpyridinium chloride (IV; R = Et, R′ = Me, X = Cl). It is presumed that, initially, chlorination occurs at the reactive 4-position, the liberated hydrogen chloride forming a salt with the base. The resulting postulated intermediate (III; R = Et, R′ = Me) could lose hydrogen chloride to give the quaternary salt. The latter is a stable water-soluble salt which is converted into the phenol-betaine (V; R = Et, R′ = Me) when treated with sodium hydrogen carbonate or one mol. of sodium hydroxide. This compound, related to the phenol-betaine derived from pyridoxine methiodide (Harris, Webb, and Folkers, *J. Amer. Chem. Soc.*, 1940, **62**, 3198), exists as a colourless hydrate which is converted into a yellow anhydrous form when dried in a vacuum or heated. Alkaline hydrolysis of the ester groups of (IV), followed by neutralisation, leads to an acid-betaine. This is not formulated since either the 4- or the 5-carboxyl group may be involved in the betaine group.



(I) (II) (III) (IV) (V)

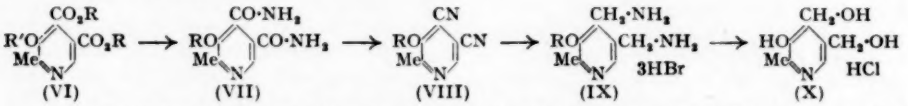
These results were applied to the synthesis of a pyridinium salt capable of conversion into a pyridine derivative, by using the *N*-benzyl compounds. Methyl α-formylsuccinate and methyl DL-α-benzylaminopropionate (cf. Bischoff, *Ber.*, 1897, **30**, 3169) gave an excellent yield of methyl *N*-benzyl-*N*-1-carbomethoxyethylaminomethylenesuccinate (I; R = Me, R′ = CH_2Ph), a high-boiling oil of remarkable thermal stability (the corresponding triethyl ester was equally stable). Dieckmann cyclisation afforded a crude cyclic keto-ester (II; R = Me, R′ = CH_2Ph), converted by the methods already mentioned, and also by direct chlorination, into 1-benzyl-4 : 5-dicarbomethoxy-3-hydroxy-2-methylpyridinium chloride (IV; R = Me, R′ = CH_2Ph, X = Cl). Bromination of the cyclic keto-ester yielded the corresponding bromide (IV; R = Me, R′ = CH_2Ph, X = Br) and these quaternary salts were also converted into the phenol-betaine (V; R = Me, R′ = CH_2Ph) by sodium hydrogen carbonate or by one equivalent of sodium hydroxide. Like the 1-methyl-betaine already mentioned, this 1-benzyl-betaine is a colourless hydrate convertible into a yellow anhydrous form. The quaternary chloride in the ethyl ester series was similarly synthesised from (I; R = Et, R′ = CH_2Ph).

Hydrogenolysis of the 1-benzylpyridinium chlorides yielded methyl and ethyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R = Me or Et, R′ = H) in the form of hydrochlorides from which the free basic esters were obtained by mild alkaline treatment. The esters were readily hydrolysed by alkali to 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylic acid (VI; R = R′ = H) (Itiba and Emoto, *Sci. Papers. Inst. Phys. Chem. Res., Tokyo*, 1941, **38**, 347). Methylation of the hydroxy-esters with diazomethane followed by hydrolysis yielded the known 3-methoxy-2-methylpyridine-4 : 5-dicarboxylic acid (Itiba and Miti, *ibid.*, 1939, **36**, 173; Kuhn *et al.*, *loc. cit.*; Harris, Stiller, and Folkers, *J. Amer. Chem. Soc.*, 1939, **61**, 1242).

Since the conversion of the tetrahydroketopyridine (II; R′ = CH_2Ph) into the 3-hydroxypyridine derivative (VI; R′ = H) involved consecutive dehydrogenation and hydrogenation, the possibility of direct conversion by a single-stage elimination of the elements of toluene was attempted by heating (II; R = Me, R′ = CH_2Ph) at low pressure. There was considerable decomposition and only a small amount of, probably, a 3-hydroxypyridine was found in the distillate (Gibbs's test).

The further conversion of the 3-hydroxypyridine diester (VI; R = Me, R′ = H) into

pyridoxine hydrochloride (cf. VI ⟶ X) was accomplished by routine procedures previously outlined by Kuhn *et al.* (*loc. cit.*). Although references to these intermediates have been made in patents (cf. U.S.P. 2,359,260, 2,371,694, 2,410,531; G.P. 701,955, 702,829) their characterisation has in some cases been meagre, and the compounds are described in the Experimental section.

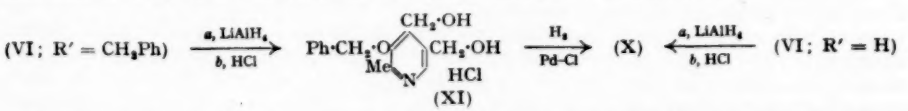


The methylation of the 3-hydroxyl group with diazomethane (VI; R′ = H ⟶ Me) and the necessary subsequent demethylation have been eliminated in an improved modification employing the principle of alkylation of phenols by a quaternary base. It was first found in model experiments that the 3-hydroxypyridine derivative (VI; R′ = H) was *O*-methylated by trimethylphenylammonium hydroxide, and that 3-hydroxypyridine yielded 3-benzyloxypyridine when heated with benzyldimethylphenylammonium hydroxide ("leucotrope"), a reaction analogous to the benzylation of phenols described by Baw (*J. Indian Chem. Soc.*, 1926, **3**, 101). By a similar procedure (VI; R = Me or Et, R′ = H) were benzylated to the 3-benzyloxypyridine diesters (VI; R = Me or Et respectively, R′ = CH_2Ph).

Attempts to achieve intramolecular *O*-benzylation of (VI; R′ = H) by thermal rearrangement of the *N*-benzyl-phenol-betaine (V; R′ = CH_2Ph) failed.

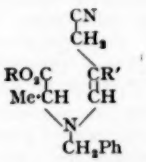
The 3-benzyloxy-esters yielded the same diamide (VII; R = CH_2Ph) which was dehydrated to the 3-benzyloxy-dinitrile (VIII; R = CH_2Ph). When this was hydrogenated to the diamine in acidic methanol, simultaneous hydrogenolysis of the benzyl group furnished directly 4 : 5-bisaminomethyl-3-hydroxy-2-methylpyridine trihydrochloride (cf. IX; R = H) which yielded pyridoxine hydrochloride (X) on treatment with nitrous acid.

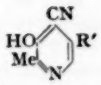
Finally, a further considerable improvement of the synthesis was effected, which eliminated the stages of the amide, nitrile, and aminomethyl derivatives, by reducing the 4 : 5-dicarboxylate groups with lithium aluminium hydride (cf. Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197). It was first found that the method could be applied to the pyridine series, by reducing ethyl nicotinate to 3-hydroxymethylpyridine (B.P. 631,078). Methyl and ethyl 3-benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R′ = CH_2Ph, R = Me and Et, respectively) were then reduced to pyridoxine benzyl ether which was readily isolated as a hydrochloride (XI) and smoothly hydrogenolysed to pyridoxine hydrochloride. Further the free 3-hydroxypyridine diester (VI; R′ = H) was similarly reduced to pyridoxine but the separtion of this amphoteric substance was inconvenient. Lithium aluminium hydride reduction of pyridinecarboxylic esters was applied to the synthesis of pyridoxine in 1947 (B.P. 629,450); similar results have since been described by Jones and Kornfeld (*J. Amer. Chem. Soc.*, 1951, **73**, 107).



Attempts at a modified synthesis were made by using substituted aminomethylenesuccinic acid derivatives obtained from *N*-benzyl-DL-alanine ester and (*a*) hydroxymethylenesuccinodinitrile (Part II, *loc. cit.*) or (*b*) ethyl β-cyano-α-formylpropionate. It was hoped that cyclisation of such compounds (XII; R′ = CN or CO_2Et) would yield, after dehydrogenation and debenzylation, the 3-hydroxypyridine derivative (XIII; R′ = CN or CO_2Et). However, treatment of (XII; R = CN) with sodium or sodium alkoxides in benzene caused only isomerisation; the elements of methanol were not eliminated (the possibility of methanol of crystallisation was excluded by suitable experiments); the product may be a dimeride of imino-nitrile character. A similarly abnormal cyclisation product of bis-2-cyanoethylmethylamine has been recorded by Cook and Reed (*J.*, 1945,

399). Treatment of (XII; R′ = CO_2Et) with sodium gave a low yield of a base, which could not be converted into a suitable 3-hydroxypyridine derivative. This approach was abandoned.

(XII) 

 (XIII)

In the course of abortive attempts to reduce the pyridine diesters with other reagents, ethyl 3-benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R = Et, R′ = CH_2Ph) was reduced by aluminium amalgam in aqueous alcohol to a dihydro-ester, a result agreeing with the similar reduction of ethyl 2 : 6-dimethylcinchomeronate to its dihydro-derivative (Mumm and Beth, *Ber.*, 1921, **54**, 1591).

Experimental

Ethyl N-1-*Carbethoxyethyl*-N-*methylaminomethylenesuccinate* (I; R = Et, R′ = Me).—A mixture of ethyl α-methylaminopropionate (30 g.) and ethyl α-formylsuccinate (46 g.) was heated at 90° for 1 hour, cooled, dissolved in ether, filtered, and freed from solvent, and the residue was distilled at low pressure. After small forerunnings of unchanged materials, the *triester* was obtained as a yellow oil, b. p. 165—170°/0·25 mm. (64·2 g., 89·5%) (Found: C, 57·1; H, 8·0; N, 4·8. $C_{15}H_{25}O_6N$ requires C, 57·2; H, 7·9; N, 4·5%).

4 : 5-*Dicarbethoxy*-3-*hydroxy*-1 : 2-*dimethylpyridinium Chloride* (IV; R = Et, R′ = Me, X = Cl).—(*a*) A solution of the foregoing compound (30 g.) in dry " AnalaR " benzene (150 ml.) was refluxed with powdered sodium (2·1 g.) under dry nitrogen. After the vigorous reaction had subsided and all sodium had dissolved, heating was continued for 1 hour. The dark solution was cooled to 0° and made just acid to litmus with aqueous acetic acid containing a little sulphuric acid. The benzene extract was separated and combined with a further ethereal extract; the combined extracts were washed with sodium hydrogen carbonate solution and water and dried (Na_2SO_4). The solvents were removed and the residual dark oil was dissolved in a slight excess of saturated anhydrous alcoholic hydrogen chloride with ice-cooling. Addition of anhydrous ether precipitated a gummy hydrochloride which was repeatedly ground with fresh dry ether till solid. Repeated recrystallisation from alcohol–ether gave the desired *pyridinium* salt (13 g.), m. p. 160—162° (decomp.), identical with that obtained as described in (*b*) (Found: Cl, 11·9. $C_{13}H_{18}O_5NCl$ requires Cl, 11·7%).

(*b*) A 20% benzene solution of ethyl *N*-1-carbethoxyethyl-*N*-methylaminomethylenesuccinate (16 g.) was refluxed with alcohol-free sodium ethoxide (from 1·7 g. of sodium). The oily product obtained from the benzene extract as described in (*a*) was dissolved in dry benzene (100 ml.) and treated dropwise with sulphuryl chloride (6 g.) at 45°. The dark oil which was precipitated was separated from the supernatant liquid and warmed at 45° at water-pump vacuum until it had completely solidified. This was triturated with dry acetone, filtered, and dried (9·8 g., 63%); recrystallised from alcohol–ether, it had m. p. 161—162° (decomp.) (Found: C, 51·4; H, 5·77; N, 4·45; Cl, 11·7. $C_{13}H_{18}O_5NCl$ requires C, 51·4; H, 5·9; N, 4·6; Cl, 11·7%).

(*c*) Cyclisation of the same starting material (16 g.) was effected with sodamide (3 g.), conditions being otherwise as in (*b*). The yield was 8·5 g.

This pyridinium salt gives a red colour with ferric chloride. When its concentrated aqueous solution was treated with sodium hydrogen carbonate or one equivalent of sodium hydroxide the corresponding *phenol-betaine* (V; R = Et, R′ = Me) separated in fine needles as a hydrated form, m. p. *ca.* 90° (Found: loss *in vacuo* over phosphoric anhydride at 56°, 9·9. $C_{13}H_{17}O_5N,1·5H_2O$ requires loss, 9·1%). The vacuum-dried yellow anhydrous *form*, crystallised from ethyl acetate, had m. p. 160° (Found: C, 59·1; H, 6·6; N, 5·3. $C_{13}H_{17}O_5N$ requires C, 58·4; H, 6·4; N, 5·2%).

Anhydro-4 : 5-*dicarboxy*-3-*hydroxy*-1 : 2-*dimethylpyridinium Hydroxide*.—A solution of the above pyridinium salt (6·1 g.) in water (20 ml.) was treated with a concentrated aqueous solution of sodium hydroxide (2·4 g.) at room temperature. After 0·5 hour the solution was acidified to litmus with acetic acid and cooled. The product was collected and recrystallised

from water, yielding the *betaine* (2·0 g.) in colourless leaflets, decomp. 230° (Found: C, 51·5; H, 4·0; N, 6·7. $C_9H_9O_5N$ requires C, 51·2; H, 4·3; N, 6·7%).

Methyl α-Benzylaminopropionate.—This *ester* was prepared by reductive condensation of alanine methyl ester with benzaldehyde, or from methyl α-bromopropionate and benzylamine as described by Bishoff (*Ber.*, 1897, **30**, 3171) for the ethyl ester; the product had b. p. 132—133°/11 mm. (Found: C, 68·8; H, 7·9; N, 7·1. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8; N, 7·25%). The *hydrochloride*, prepared in the usual way, crystallised from methanol–ether in needles, m. p. 177° (decomp.) (Found: Cl, 15·4. $C_{11}H_{16}O_2NCl$ requires Cl, 15·5%).

Methyl N-Benzyl-N-1-carbomethoxyethylaminomethylenesuccinate (I; R = Me, R′ = CH_2Ph). —A mixture of methyl α-formylsuccinate (17·4 g.) and methyl α-benzylaminopropionate (19·5 g.) was heated at 100° for 1·5 hours and left to cool overnight. An ether solution of the viscous product was washed with sodium hydrogen carbonate and water, dried, and evaporated, and the residue distilled. The *product*, a deep yellow viscous oil (27·4 g.), had b. p. 195—198°/0·35 mm. (Found: C, 62·6; H, 6·8; N, 4·2. $C_{18}H_{23}O_6N$ requires C, 62·0; H, 6·6; N, 4·0%).

Ethyl N-Benzyl-N-1-carbethoxyethylaminomethylenesuccinate (I; R = Et, R′ = CH_2Ph) was similarly prepared from ethyl α-formylsuccinate in 90% yield, forming a similar viscous oil, b. p. *ca.* 210°/0·3 mm. (Found: N, 3·6. $C_{21}H_{29}O_6N$ requires N, 3·58%).

1-Benzyl-4 : 5-dicarbomethoxy-3-hydroxy-2-methylpyridinium Chloride (IV; R = Me, R′ = CH_2Ph).—(*a*) A solution of the above trimethyl ester (36 g.) in dry " AnalaR " benzene (150 ml.) was refluxed with sodium powder (2·4 g.) in an atmosphere of nitrogen. The sodium gradually dissolved with formation of a dark reddish solution, initial reaction being hastened by addition of a trace of sodium ethoxide. Heating was continued for 1 hour after dissolution of the sodium. The mixture was cooled to 0° and acidified to litmus with acetic acid and ice. Combined benzene extracts of the product were washed with sodium hydrogen carbonate, and water, and dried (Na_2SO_4). After removal of benzene under reduced pressure, the residual oil (*ca.* 33 g.) was treated with an equivalent quantity of saturated absolute alcoholic hydrogen chloride, and the hydrochloride precipitated with anhydrous ether as a gum. This was separated by decantation and redissolved in methanol. Anhydrous ether was added till the solution was just turbid and the mixture was kept at room temperature for some days, with gradual addition of further amounts of dry ether as the crystalline quaternary chloride separated. A preferable procedure is to digest the primary ether-precipitated hydrochloride with dry ether, decant the liquid, and expose the residue to dry air for a few days. On addition of dry acetone the pigmented material was dissolved, leaving the quaternary *chloride* as a crystalline product. It crystallised from methanol–ether in colourless prisms, m. p. 148—150° (decomp.) (Found: C, 58·3; H, 5·3; Cl, 10·0; N, 4·0. $C_{17}H_{18}O_5NCl$ requires C, 58·0; H, 5·1; Cl, 10·1; N, 4·0%).

(*b*) The above cyclisation was carried out on the same scale with the equivalent amount of alcohol-free sodium methoxide (5·55 g.). The benzene extract of the free cyclic keto-ester was dried, filtered, and partly evaporated to remove traces of water. This solution was stirred and treated dropwise with sulphuryl chloride (12 g.) at 40°. A dark oil separated and, after it had settled, the benzene was decanted and the oil washed with a little more benzene. The oil was warmed at 40° at the water-pump for 2 hours. The resulting frothy mass was digested with warm dry acetone (50 ml.), leaving the pyridinium chloride as a slightly pink crystalline solid, identical with that obtained as described in (*a*) (yield, 22·5 g., 62%).

(*c*) Similar results were obtained by cyclisation with an equivalent amount of sodamide.

Dehydrogenations with Halogens.—(a) *Chlorine.* After cyclisation with sodium methoxide as described above [(*b*)], the crude, dried cyclic keto-ester was treated in benzene solution with a N-solution of chlorine in carbon tetrachloride (100 ml.) with stirring at room temperature. After settling, the oil which had precipitated gradually was separated by decantation and gently warmed *in vacuo*. The residue was digested with warm acetone (20 ml.), leaving 1-benzyl-4 : 5-dicarbomethoxy-3-hydroxy-2-methylpyridinium chloride, m. p. and mixed m. p. 149° (decomp.) (4·0 g.).

(b) *Bromine.* A solution of the crude cyclic keto-ester obtained with sodium methoxide from (I; R = Me, R′ = CH_2Ph) (35 g.) in dry benzene (200 ml.) was stirred at 0° and a solution of bromine (16 g.) in carbon tetrachloride (100 ml.) was added gradually. A light brown viscous gum was precipitated and this process appeared to be complete when about 60 ml. of bromine solution had been added. Bromine addition was stopped, any excess of bromine was removed in a stream of dry nitrogen, and the benzene decanted. The residue became more mobile, and deep red, as hydrogen bromide was evolved freely. It was kept at water-pump vacuum for

some hours and treated with warm acetone (25 ml.). When solid began to separate, dry ether (50 ml.) was added gradually with shaking. After 4 hours the precipitated solid was filtered off, washed with acetone–ether, and dried *in vacuo* (yield, 18·2 g., 52%). Recrystallisation from methanol–ether gave 1-*benzyl*-4 : 5-*dicarbomethoxy*-3-*hydroxy*-2-*methylpyridinium bromide*, colourless prisms, m. p. 134—135° (decomp.) (Found : C, 52·1; H, 4·9; N, 3·4; Br, 20·0. $C_{17}H_{18}O_5NBr$ requires C, 51·5; H, 4·5; N, 3·5; Br, 20·2%).

This bromide is readily converted into the corresponding chloride, identical with that described above, by shaking it in methanol solution with excess of freshly prepared silver chloride.

When a solution of the quaternary chloride (7·03 g.) in water (15 ml.) was treated with 2N-sodium hydroxide (10 ml.) at 0°, the *phenol-betaine* (V; R = Me, R′ = CH_2Ph) crystallised (6·15 g.). It recrystallised from water in colourless flat needles or prisms which are hydrated, losing *ca.* 3·3% by weight on vacuum-drying over phosphoric anhydride at 66°, then becoming yellow and having m. p. 138—140° (purple-red liquid) (Found : N, 4·3. $C_{17}H_{17}O_5N$ requires N, 4·4%).

1-*Benzyl*-4 : 5-*dicarbethoxy*-3-*hydroxy*-2-*methylpyridinium Chloride* (IV; R = Et, R′ = CH_2Ph).—Cyclisation of (I; R = Et, R′ = CH_2Ph) was carried out with sodium ethoxide as described for the methyl ester, and sulphuryl chloride was used for dehydrogenative chlorination. The product was somewhat soluble in warm acetone but could be purified by digestion with ethyl acetate. Recrystallisation from acetone–ether gave the *pyridinium* salt as colourless needles, m. p. 135—136° (decomp.) (Found : C, 60·0; H, 5·9; N, 4·25; Cl, 9·4. $C_{19}H_{22}O_5NCl$ requires C, 60·1; H, 5·80; N, 3·7; Cl, 9·3%).

Dimethyl 3-*Hydroxy*-2-*methylpyridine*-4 : 5-*dicarboxylate Hydrochloride*.—A solution of 1-benzyl-4 : 5-dicarbomethoxy-3-hydroxy-2-methylpyridinium chloride (35·15 g.) in methanol (120 ml.) was shaken with palladium–charcoal (4 g.; 1 : 10) in hydrogen at room temperature and slightly >1 atm. After 2·5 l. of hydrogen had been absorbed in 1 hour, hydrogenation ceased. The catalyst was filtered off and the solution evaporated to small volume under reduced pressure. The crystalline salt was collected, washed with dry ether, and dried (23·4 g.; m. p. *ca.* 153°). From methanol–ether, it separated in colourless needles, m. p. 165—168° (decomp.) (Found : C, 46·6; H, 4·7; N, 5·25; Cl, 13·4. $C_{10}H_{12}O_5NCl$ requires C, 45·9; H, 4·6; N, 5·35; Cl, 13·6%). Another form of the hydrochloride, with m. p. 223° (decomp.), showed the same composition and yielded the identical free base.

The hydrochloride (either form) (28·8 g.) was treated in a minimal amount of water at 0° with powdered sodium hydrogen carbonate till the solution was slightly alkaline. The precipitated *base* was filtered off, washed with ice water, and dried. A further crop was obtained by salting out of the filtrate and extraction with ether. The total yield was 16·5 g. Recrystallisation from light petroleum (b. p. 60—80°) or methanol gave colourless felted needles, m. p. 138—140° (Found : C, 53·3; H, 4·9; N, 6·3. $C_{10}H_{11}O_5N$ requires C, 53·4; H, 4·9; N, 6·2%).

When the hydrochloride (5 g.) in dry pyridine (50 ml.) was treated with toluene-*p*-sulphonyl chloride (3·8 g.) at room temperature for 24 hours, *methyl* 2-*methyl*-3-*toluene*-p-*sulphonyloxy*-*pyridine*-4 : 5-*dicarboxylate* was obtained. It was precipitated by water from the reaction mixture, dried (6 g.), and recrystallised from methanol in colourless rectangular prisms, m. p. 99—100° (Found : C, 53·55; H, 4·6; N, 3·7. $C_{17}H_{17}O_7NS$ requires C, 53·8; H, 4·5; N, 3·7%). By the action of concentrated aqueous ammonia, this compound undergoes slow reaction at all three ester groups with formation of 3-*hydroxy*-2-*methylpyridine*-4 : 5-*dicarboxyamide* in low yield. Unchanged ester was filtered off from the ammonia solution, and the solution evaporated to dryness. Recrystallisation from methanol gave pale yellow prisms, slowly decomposing above 250° (Found : N, 22·0. $C_8H_9O_3N_3$ requires N, 21·6%). Direct treatment of methyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylate with ammonia (*d* 0·88) resulted in hydrolysis of at least one ester group, as well as amidation, and only mixed products containing ammonium salts of half-amides were obtained. The hydroxy-diamide was also formed by the following indirect but more reliable route. The betaine (V; R′ = CH_2Ph, R = Me) (3·15 g.) was finely powdered and added to ice-cold ammonia (*d* 0·88; 15 ml.). After being kept overnight, the brownish suspension of solid was filtered off and the product washed with cold water and dried (2·1 g.). Purification was effected by dissolution in dilute hydrochloric acid, filtration (charcoal), and reprecipitation with sodium hydrogen carbonate, yielding buff crystals, m. p. 255—257° (decomp.), of *anhydro*-1-*benzyl*-4 : 5-*dicarbamyl*-3-*hydroxy*-2-*methylpyridinium hydroxide* (Found : Total N, 13·9; amide-N, 9·8. $C_{15}H_{15}O_3N_3$ requires 14·7 and 9·8%, respectively). When this was hydrogenolysed in methanol containing hydrochloric acid, with palladised charcoal as catalyst, 3-*hydroxy*-2-*methylpyridine*-4 : 5-*dicarboxyamide hydrochloride*

was obtained, decomp. >200° (Found: Cl′, 14·9. $C_8H_{10}O_3N_2Cl$ requires Cl′, 15·3%). When treated with dilute sodium hydrogen carbonate solution the free hydroxy-diamide crystallised in pale yellow prisms, identical with that described above.

Diethyl 3-*Hydroxy*-2-*methylpyridine*-4 : 5-*dicarboxylate Hydrochloride*.—A solution of 1-benzyl-4 : 5-dicarbethoxy-3-hydroxy-2-methylpyridinium chloride (20 g.) in ethanol (80 ml.) was hydrogenated as described for the corresponding methyl ester. Evaporation of the filtered solution under reduced pressure to low volume yielded the product (11·1 g.) which crystallised from alcohol–ether in colourless needles, m. p. 144—145° (Found: C, 49·9; H, 5·55; N, 5·1. $C_{12}H_{16}O_5NCl$ requires C, 49·7; H, 5·5; N, 4·8%). The corresponding base was obtained as a low-melting solid which was not further purified but could be satisfactorily used in further operations. This ester as well as the dimethyl ester was readily hydrolysed by brief heating in dilute sodium hydroxide solution on the water-bath. The solution, just acidified to Congo-red, deposited 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylic acid, m. p. 259° (decomp.) after recrystallisation from water (Found: C, 48·9; H, 3·7. Calc. for $C_8H_7O_5N$: C, 48·7; H, 3·6%).

Dimethyl 3-*Methoxy*-2-*methylpyridine*-4 : 5-*dicarboxylate* (VI; R = R′ = Me).—(*a*) The 3-hydroxypyridine derivative (11·25 g.) was added at 0° to ethereal diazomethane [from nitroso-methylurethane (15 ml.)], and kept at 3—5° for 3 days while most of the solid dissolved with evolution of nitrogen. The filtered solution was freed from excess of diazomethane and ether, and the residual oil distilled at 114—116°/0·5 mm. (8 g.) (Found: C, 55·55; H, 5·5; N, 5·6. Calc. for $C_{11}H_{13}O_5N$: C, 55·3; H, 5·4; N, 5·8%). Ichiba, Michi, and Emoto (*Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1941, **39**, 126) record m. p. 40—41°. The present material was satisfactorily amidated as shown below.

(*b*) Methyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylate was treated in methanol with one equivalent of sodium methoxide. Addition of excess of dry ether precipitated the sodium salt which was filtered off and dried *in vacuo*. A solution of this salt (10·5 g.) in methanol (25 ml.) was mixed with one of trimethylphenylammonium chloride (8 g.) in methanol (15 ml.), and the mixture added, during 10 minutes, to boiling xylene (100 ml.) which was stirred in an atmosphere of nitrogen in an apparatus arranged to distil off the methanol and a little xylene. After 1 hour's heating the xylene solution was filtered from sodium chloride, washed with sodium hydrogen carbonate, and dried. After removal of xylene and dimethylaniline under reduced pressure, the residual oil was distilled yielding the product (5·9 g., 71%), b. p. 109—112°/0·2 mm. (Found: C, 55·1; H, 5·7; N, 6·0. Calc. for $C_{11}H_{13}O_5N$: C, 55·3; H, 5·4; N, 5·8%).

3-*Methoxy*-2-*methylpyridine*-4 : 5-*dicarboxyamide* (VII; R = Me).—This was obtained from the crude methoxy-diester by keeping its solution in liquid ammonia for 2 days. After evaporation, the residue was recrystallised from methanol, yielding small colourless leaflets (>90% yield) (Found: total N, 20·15; amide-N, 13·0. Calc. for $C_9H_{11}O_3N_3$: total N, 20·1; amide-N, 13·4%) which decompose at 210°, with liberation of ammonia and formation of the imide which melts about 250° (cf. Ichiba *et al.*, *loc. cit.*). The latter is reconverted into the diamide by concentrated ammonia.

4 : 5-*Dicyano*-3-*methoxy*-2-*methylpyridine* (VIII; R = Me).—The methoxy-diamide (10 g.) was added gradually to a stirred mixture of dry benzene (31 ml.), dry pyridine (31 ml.), and phosphorus oxychloride (7·9 g.) at 0—5°. The bath was gradually heated and finally kept at 60—70° for 1 hour. The dark mixture was mixed with ice and excess of sodium acetate, and benzene and pyridine were removed under reduced pressure. The aqueous residue was cooled and the solid filtered off and dried (5·1 g.). This was purified by vacuum-sublimation and recrystallised from aqueous methanol from which it separated in flat needles, m. p. 78° (Found: C, 62·3; H, 3·85; N, 24·4. Calc. for $C_9H_7ON_3$: C, 62·4; H, 4·05; N, 24·2%). Kuhn *et al.* (*loc. cit.*) gave m. p. 70°.

4 : 5-*Bisaminomethyl*-3-*methoxy*-2-*methylpyridine Trihydrochloride* (cf. IX; R = Me).—A solution of 4 : 5-dicyano-3-methoxy-2-methylpyridine (2·5 g.) in methanol (180 ml.) was dripped into a suspension of palladium chloride (1·5 g.) in methanol (50 ml.) acidified with dilute hydrochloric acid, with shaking in a hydrogen atmosphere. Hydrogen was absorbed fairly readily with formation of a pale yellow solution with intense blue fluorescence. The solution was filtered until clear, partly concentrated, and treated with anhydrous ether which precipitated the product as a *trihydrochloride hemihydrate*; this crystallised from methanol–ether in colourless leaflets, decomp. 200°, readily soluble in water (slightly acid to Congo-red) and sparingly soluble in alcohol (Found: C, 35·8; H, 6·8; N, 13·9; Cl, 35·1. $C_9H_{18}ON_3Cl_3,0·5H_2O$ requires C, 36·05; H, 6·4; N, 14·0; Cl, 35·6%).

4 : 5-*Bisaminomethyl*-3-*hydroxy*-2-*methylpyridine Trihydrobromide* (IX; R = H).—A solution of the above methoxy-compound (5·8 g.) in concentrated hydrobromic acid (*d* 1·5; 145 ml.) was

refluxed for 30 minutes, cooled, mixed with alcohol (200 ml.), and treated with ether (250 ml.). The *trihydrobromide* which crystallised on chilling was collected and washed with alcohol–ether (yield, 7·5 g.). It is sparingly soluble in alcohol and can be recrystallised from aqueous alcohol by addition of ether; it decomposes at about 280° (Found: Br′, 58·7. $C_8H_{16}ON_2Br_3$ requires Br′, 58·5%).

Demethylation with concentrated hydrochloric acid at 130° for 4 hours yielded a product containing about 12% of residual methoxy-compound.

3-Benzyloxypyridine.—A solution of 3-hydroxypyridine (0·95 g.) in methanol (5 ml.) was mixed with a solution of sodium (0·23 g.) in methanol (5 ml.), and to this was added a solution of benzyldimethylphenylammonium chloride (2·5 g.) in methanol (5 ml.). The whole was added gradually to boiling xylene in a bath at 150—160°, as described for the similar methylation of the 3-hydroxypyridine diester above. Similar working up yielded the product as an oil, b. p. 114°/0·6 mm. (0·7 g.). This gave *3-benzyloxypyridinium picrate*, yellow needles (from ethanol), m. p. 118—120° (Found: C, 52·5; H, 3·4; N, 13·8. $C_{18}H_{14}O_8N_4$ requires C, 52·2; H, 3·4; N, 13·5%).

Methyl 3-Benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R = Me, R′ = CH_2Ph).—A solution of methyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylate hydrochloride (13 g.) in methanol (30 ml.) was treated with a solution of sodium (2·3 g., 2 equivs.) in methanol (25 ml.) and then mixed with a solution of benzyldimethylphenylammonium chloride (12·1 g.) in methanol (15 ml.). The whole was added to boiling xylene (100 ml.) as described above and heating continued for 1 hour. The *product* was obtained by vacuum-distillation, having b. p. 173—176°/0·3 mm. (12·4 g., 80%), and crystallised from light petroleum (b. p. 60—80°) in colourless needles, m. p. 68° (Found: C, 64·9; H, 5·5; N, 4·6. $C_{17}H_{17}O_5N$ requires C, 64·7; H, 5·4; N, 4·4%).

Ethyl 3-Benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R = Et, R′ = CH_2Ph).—This *ester* was prepared in 80% yield as described for the dimethyl ester. It had b. p. 187—189°/0·3 mm., and crystallised from light petroleum (b. p. 40—60°) in colourless prisms, m. p. 48—49° (Found: C, 65·8; H, 6·1; N, 4·1. $C_{19}H_{21}O_5N$ requires C, 66·4; H, 6·1; N, 4·1%).

3-Benzyloxy-2-methylpyridine-4 : 5-dicarboxyamide (VII; R = CH_2Ph).—Methyl 3-benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (11·2 g.) was gradually added to liquid ammonia (30 ml.), and the mixture kept sealed at room temperature for 3 days. After evaporation of the ammonia, the product was digested with ether, filtered, and recrystallised from methanol in pale cream-coloured leaflets which decomposed at 194° with evolution of ammonia (Found: N, 15·2. $C_{15}H_{15}O_3N_3$ requires N, 14·7%). This *amide* was identical with the product obtained by treatment of methyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylate with diazotoluene, followed by amidation with liquid ammonia.

3-Benzyloxy-4 : 5-dicyano-2-methylpyridine (VIII; R = CH_2Ph).—The above diamide, finely powdered (9·4 g.), was gradually added to a stirred mixture of dry pyridine (27 ml.), dry benzene (13·6 ml.), and phosphoryl chloride (8·5 g.), cooled in ice-water. The temperature was slowly raised to 30°, whereupon the mixture became dark purple. This was then vigorously stirred at 65—70° for 1 hour, cooled to 0°, and mixed with crushed ice (40 g.). Benzene and pyridine were removed under reduced pressure and the solid which had separated was filtered off, washed with water, and dried *in vacuo* (5·1 g.). Vacuum-sublimation (90—95°/10^{-5} mm.) yielded the pale yellow crystalline *dinitrile*, m. p. 96° (Found: N, 16·6. $C_{15}H_{11}ON_3$ requires N, 16·9%).

4 : 5-Bisaminomethyl-3-hydroxy-2-methylpyridine Trihydrochloride (cf. IX; R = H).—A solution of the foregoing benzyloxy-dinitrile (3·95 g.) in methanol (115 ml.) containing concentrated hydrochloric acid (5·5 ml.) was added in 6 portions to a suspension of active palladium–charcoal (1 : 10; 1 g.) in methanol (20 ml.) and shaken in hydrogen. The initial hydrogen consumption corresponding to debenzylation was rapid but slowed down until, after 20—25 minutes, 5 mols. of hydrogen had been absorbed. Finally a total uptake of about 2 l. of hydrogen was recorded. The solution, filtered from catalyst, yielded the trihydrochloride (1·85 g.) when chilled and a further crop of 2·05 g. was obtained by evaporating the solution to dryness and triturating the residue with absolute alcohol. The product crystallised as a *trihydrate* (from aqueous alcohol) in flat needles, decomposing above 280° with partial sublimation (Found: loss at 100°, 10·7. $C_8H_{16}ON_3Cl_3,3H_2O$ requires loss, 11·5%. Found, in anhydrous material: N, 15·5; Cl, 37·9. $C_8H_{16}ON_3Cl_3$ requires N, 15·2; Cl, 38·5%).

Reductions with Lithium Aluminium Hydride.—3-Hydroxymethylpyridine. A solution of ethyl nicotinate (15·1 g.) in dry ether (30 ml.) was added slowly to a vigorously stirred suspension of lithium aluminium hydride (2·4 g.) in dry ether (100 ml.) at 0—5°. The gummy yellow

precipitate was stirred for a further hour at 0°, decomposed with ice-water (50 ml.), and treated with excess of sodium hydroxide. The mixture was continuously extracted with ether from which was obtained some unchanged ethyl nicotinate (0·8 g.) and 3-hydroxymethylpyridine (2·35 g.), b. p. 141—146°/15 mm. Redistillation gave material of b. p. 142—143°/15 mm., $n_D^{18\cdot5}$ 1·5451, in agreement with known constants, and the picrate had m. p. 158—160° not depressed on admixture with authentic material.

3-Benzyloxy-4 : 5-bishydroxymethyl-2-methylpyridine (cf. XI).—A solution of ethyl 3-benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (17·15 g.) in dry ether (50 ml.) was added slowly to lithium aluminium hydride (4 g.) in dry ether (250 ml.) as described above. After 1¾ hours, the mixture was decomposed with ice-water (300 ml.), and 50% aqueous sodium hydroxide (75 ml.) was added. Continuous ether-extraction (16 hours) yielded 2·8 g. of product but the alumina retained a considerable proportion which was only removed by filtering it off, drying it, and extracting it with boiling ethyl acetate and chloroform. In this way further crops of product were isolated. The total yield was 6·75 g. (52%). Recrystallisation from benzene or ethyl acetate gave colourless prisms, m. p. 118—120° (Found: C, 69·3; H, 6·65; N, 5·5. $C_{15}H_{17}O_3N$ requires C, 69·5; H, 6·5; N, 5·4%).

When the reduction mixture (same scale as above) was worked up by the addition of ice-cold 5N-hydrochloric acid (60 ml.), inorganic material was dissolved and the product separated in the form of *3-benzyloxy-4 : 5-bishydroxymethyl-2-methylpyridine hydrochloride* (12·7 g., 85%) which, crystallised from alcohol–ether, had m. p. 178° (Found: N, 4·6; Cl, 12·3. $C_{15}H_{18}O_3NCl$ requires N, 4·7; Cl, 12·0%).

4 : 5-Bishydroxymethyl-3-methoxy-2-methylpyridine (*Pyridoxine Methyl Ether*).—A solution of ethyl 3-methoxy-2-methylpyridine-4 : 5-dicarboxylate (5·7 g.) in dry ether (25 ml.) was similarly reduced with lithium aluminium hydride (1·3 g.). Ethereal extracts of the alkaline decomposition mixture yielded an oil which, crystallised from ethyl acetate, had m. p. 102—104° (Stiller *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 1240, give m. p. 101—102°) (Found: N, 7·3. Calc. for $C_9H_{13}O_3N$: N, 7·65%).

3-Hydroxy-4 : 5-bishydroxymethyl-2-methylpyridine Hydrochloride (*Pyridoxine Hydrochloride*) (X).—(*a*) A solution of ethyl 3-hydroxy-2-methylpyridine-4 : 5-dicarboxylate (12 g.) in dry ether (50 ml.) was dropped into lithium aluminium hydride (5 g.) in dry ether (300 ml.), vigorously stirred at 0° in nitrogen. The pale yellow precipitate was stirred for 1½ hours and left overnight at room temperature. To the mixture were added ice-water (100 ml.) and an aqueous solution (50 ml.) of sodium hydroxide (21 g.). The alkaline mixture was saturated with carbon dioxide and continuously extracted with ether (2 days). The residue after removal of ether from the extract was dissolved in a small volume of absolute alcohol and treated with ethereal hydrogen chloride, yielding pyridoxine hydrochloride (2·3 g.) as a light brown crystalline powder, m. p. 202° (decomp.). It was identified as such by direct comparison with authentic material.

The ethereal reaction mixture obtained as just described was gently refluxed with acetic anhydride (30 ml.) for 2 hours. The ether was evaporated and acetic anhydride (30 ml.) again added. The mixture was heated on the water-bath for some hours, then filtered hot, and excess of acetic anhydride and more volatile material were removed under reduced pressure. The residue was fractionated, yielding pyridoxine triacetate (6·0 g.), b. p. 145—150°/0·5 mm. (Found, on material redistilled at 148°/0·5 mm.: C, 56·96; H, 5·7; N, 4·9. Calc. for $C_{14}H_{17}O_6N$: C, 56·95; H, 5·8; N, 4·75%).

(*b*) A solution of 3-benzyloxy-4 : 5-bishydroxymethyl-2-methylpyridine hydrochloride (43·5 g.) in warm water (500 ml.) was hydrogenated by shaking it with 10% palladised charcoal (6·0 g.; prepared by reduction of palladium chloride–charcoal suspension in sodium acetate solution, filtered off, and washed with water) in hydrogen, of which 3060 ml. were absorbed. After filtration from the catalyst the solution was evaporated under reduced pressure to dryness and the residue (28·2 g.) recrystallised from concentrated aqueous solution; it had m. p. 208—210° (decomp.) and was identical with authentic pyridoxine hydrochloride (Found: C, 47·1; H, 6·05; N, 6·7; Cl, 17·7, 17·4. Calc. for $C_8H_{12}O_3NCl$: C, 46·7; H, 5·8; N, 6·8; Cl, 17·3%).

(*c*) A solution of 4 : 5-bisaminomethyl-3-hydroxy-2-methylpyridine trihydrobromide (4·1 g.) in water (40 ml.) was stirred at 100° for 1 hour with an excess of freshly prepared, washed silver chloride, and filtered clear from silver bromide and residual chloride. The filtrate was stirred with 2N-hydrochloric acid (80 ml.) at 30° while a solution of sodium nitrite (1·7 g.) in water (17 ml.) was run in. The mixture was then heated at 90° for 20 minutes. It was evaporated to dryness under reduced pressure and the dry residue extracted several times with boiling absolute alcohol. The extract, filtered from sodium chloride, was chilled overnight and the pyridoxine

hydrochloride which crystallised was filtered off, washed with acetone, and vacuum-dried (yield, 1·2 g., 58%; m. p. 204—208°). Recrystallisation as above provided pure pyridoxine hydrochloride. Small crops of less pure product separated from the alcoholic mother-liquor when concentrated, the final mother-liquor being set aside for isolation of a by-product (see succeeding paper).

Ethyl 3-Benzyloxy-2-methyldihydropyridine-4 : 5-dicarboxylate.—Aluminium amalgam, freshly prepared from cut metal foil (5 g.), was added to ethyl 3-benzyloxy-2-methylpyridine-4 : 5-dicarboxylate (VI; R = Et, R′ = CH_2Ph) (17·15 g.) in alcohol (100 ml.). Water (10 ml.) was added and the mixture refluxed for 45 minutes. Alcohol (50 ml.) and water (5 ml.) were again added and refluxing was continued for an hour. The filtered solution was mixed with a boiling alcoholic extract of the alumina residue, and the combined solutions were evaporated to dryness under reduced pressure. The residual solid (16·1 g.) recrystallised from ethyl acetate–light petroleum (b. p. 60—80°) as fine colourless needles, m. p. 102—104°, with an intense blue fluorescence in ultra-violet light (Found: C, 66·1; H, 6·95. $C_{19}H_{23}O_5N$ requires C, 66·1; H, 6·7%).

Methyl α-(N-Benzyl-N-1-carbomethoxyethylaminomethylene)-β-cyanopropionate (XII; R = Me, R′ = CO_2Me).—Methyl β-cyano-α-formylpropionate (9·5 g.) and methyl α-benzylaminopropionate (13 g.) were heated on a steam-bath for 1 hour, cooled, and digested with ether. Insoluble material, probably the diketopiperazine from the amino-ester, was filtered off, and, after removal of the ether, the residual oil was distilled, yielding, after a lower-boiling fraction of mixed unchanged materials (5 g.), the ester (12·5 g.) as a viscous yellow oil, b. p. 203—205°/0·1 mm. (Found: C, 64·5; H, 6·4; N, 8·8. $C_{17}H_{20}O_4N_2$ requires C, 64·5; H, 6·3; N, 8·9%).

N-Benzyl-N-1-carbomethoxyethylaminomethylenesuccinonitrile (XII; R = Me, R′ = CN).—An intimate mixture of methyl α-benzylaminopropionate hydrochloride (45·9 g.) and potassium α-hydroxymethylenesuccinonitrile (29·5 g.; see Part II, *loc. cit.*) was heated at 105—115° for 3 hours under nitrogen. The dark melt was extracted with boiling benzene and filtered, and the extract washed with water, sodium hydrogen carbonate solution, water again, and dried (Na_2SO_4). After removal of the solvent and material volatile at up to 150°/0·1 mm., the residue was degassed at low pressure and submitted to short-path distillation, yielding a viscous oily *nitrile* (23·1 g.) at 140—150°/5 × 10^{-4} mm. (Found: N, 15·0. $C_{16}H_{17}O_2N_3$ requires N, 14·8%).

Cyclisation Attempts.—A solution of the last-mentioned nitrile (10 g.) in dry "AnalaR" benzene (100 ml.) was refluxed with sodium powder (0·9 g.) under nitrogen for 1·5 hours. The resulting dark solution was cooled and shaken at 0° under nitrogen with sufficient ice-cold dilute acetic acid containing a little dilute sulphuric acid to render the mixture just acid to litmus. The benzene extract was washed free of acid and dried ($MgSO_4$). Addition of anhydrous methanolic hydrogen chloride (*ca.* 1 equiv.) precipitated first an oil, from which the solution was decanted, and then a crystalline hydrochloride which was collected, washed with acetone, and dried (2·2 g.). Recrystallisation from alcohol–ethyl acetate yielded colourless fibrous needles, m. p. 197° (decomp.) (Found: C, 60·1; H, 5·4; N, 13·0; Cl, 11·2. $C_{16}H_{17}O_2N_3$,HCl requires C, 60·2; H, 5·6; N, 13·1; Cl, 11·1%). A pure specimen of this *salt*, heated for some hours at 140° *in vacuo*, showed no loss of methanol and gave the same analytical figures. That the substance was not the hydrochloride (m. p. 117·5°) of the starting material was shown by a considerable m. p. depression.

The same product was obtained in similar experiments with sodium methoxide, potassium ethoxide, and sodium *iso*amyloxide, and when the use of methanol in working up was avoided.

In one experiment with sodium, the first, oily fraction of hydrochloride (cf. above) eventually crystallised from methanol–ether, and had m. p. 190—192°, depressed to 170° by the product already described. The *substance* was oxygen-free and analysis also indicated elimination of a carbomethoxy-group (Found: C, 64·7; H, 6·7; N, 15·3; Cl, 13·5. $C_{14}H_{15}N_3$,HCl requires C, 64·2; H, 6·1; N, 16·1; Cl, 13·6%).

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839. *Synthetical Experiments in the B Group of Vitamins. Part V.* Novel Derivatives of Pyridoxine.*

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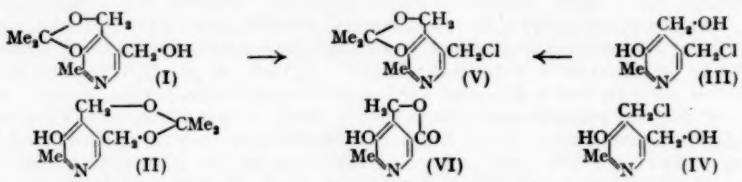
Pyridoxine hydrochloride yields an *iso*propylidene derivative (I) which provides a novel means of protection for the phenolic and 4-hydroxymethyl groups. A by-product in the conversion of 4 : 5-bisaminomethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine into pyridoxine hydrochloride is 5-chloromethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine (III). The structural relation between (I) and (III) is demonstrated by the chlorination of the former to a product (V), identical with the *iso*propylidene derivative of (III).

Pyridoxine hydrochloride and acetone in the presence of sulphuric acid form an *iso*propylidene derivative, isolated as a hydrochloride $C_{11}H_{15}O_3N,HCl$. Of the possible structures (I) and (II) for the free base, the former was to be preferred since, apart from the less likely seven-membered ring in (II), involvement of the phenolic group is shown by a negative test with the 2 : 6-dichloroquinone-chloroimide reagent for a phenol with a free *para*-position; the test rapidly becomes positive when the compound is warmed with aqueous acid, which regenerates pyridoxine hydrochloride. In alkaline solution, *iso*propylidenepyridoxine is stable, in analogy with *iso*propylidene derivatives of sugars. The structure (I) has been confirmed by alkaline permanganate oxidation which yields, after acid hydrolysis, the known lactone (VI) of 3-hydroxy-4-hydroxymethyl-2-methylpyridine-5-carboxylic acid (cf. Harris, Stiller, and Folkers, *J. Amer. Chem. Soc.*, 1939, **61**, 1242).



This preparation of (I) is believed to be the first instance of the simultaneous protection of phenolic and alcoholic hydroxyl groups by cyclic ketal formation commonly used in carbohydrate chemistry, and should be more generally applicable to other aromatic compounds with these substituent groups similarly located. The *cyclo*hexylidene derivative of pyridoxine has also been prepared. It leaves the 5-hydroxymethyl group free for further reactions such as oxidation and esterification. Phosphorylation of this group is described by Baddiley and Mathias (*J.*, 1952, 2583) in the course of a synthesis of codecarboxylase, and further experiments relating to similar work will be reported later.

When 4 : 5-bisaminomethyl-3-hydroxy-2-methylpyridine is treated with sodium nitrite in hydrochloric acid solution for conversion into pyridoxine hydrochloride (preceding paper), the latter is extracted from the dry residue of the evaporated solution by absolute alcohol; sodium chloride is filtered off and pyridoxine hydrochloride crystallises. From the alcoholic mother-liquors there has been isolated a by-product in the form of an alcohol-soluble hydrochloride, $C_8H_{10}O_2NCl,HCl$, m. p. 170—171°. The base is 5-chloromethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine (III), since it is a free phenol, and the alternative 4-chloromethyl compound (IV) is excluded by the ready formation of an *iso*propylidene derivative (V). Moreover, this *iso*propylidene derivative is identical with the chlorination product of (I). The structures of (I) and (III) are thus mutually confirmatory. It is not known whether the formation of (III) is due to a side reaction in which hydrochloric acid reacts with pyridoxine, or one in which some nitrosyl chloride is formed which chlorinates the 5-hydroxymethyl group. It has been found difficult to demonstrate

* Part IV, preceding paper.

unequivocally the formation of (III) by treatment of pyridoxine with even concentrated hydrochloric acid.

In microbiological assay with *Neurospora sitophila* (mutant 299) (III) has about one quarter of the activity of pyridoxine hydrochloride.

When treated with excess of diethylamine, (III) is converted into 5-diethylaminomethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine, characterised as a dipicrate and dihydrochloride. The latter salt has little or no spasmolytic activity against histamine on isolated guinea-pig gut.

Experimental

iso*Propylidenepyridoxine*.—Pyridoxine hydrochloride (2 g.) was stirred with acetone (40 ml.) containing concentrated sulphuric acid (4 ml.) until dissolved. The solution was kept at room temperature overnight and treated with a solution of sodium (5·9 g.) in ethanol (100 ml.). The precipitated sodium sulphate was filtered off and washed with ethanol, and the filtrate evaporated to dryness under reduced pressure. The residue was extracted with ethanol and treated with anhydrous alcoholic hydrogen chloride and acetone, yielding iso*propylidenepyridoxine hydrochloride* (1·6 g.) which, crystallised from alcohol–ether, had m. p. 217—218° (decomp.) (Found: C, 53·0; H, 6·4; N, 5·6. $C_{11}H_{16}O_3NCl$ requires C, 53·6; H, 6·5; N, 5·7%). The base was liberated from the hydrochloride by aqueous sodium hydrogen carbonate and recrystallised from faintly ammoniacal water in colourless needles, m. p. 113—115° (Found: C, 64·0; H, 6·4; N, 7·1. $C_{11}H_{15}O_3N$ requires C, 63·2; H, 7·2; N, 6·7%). Pure *iso*propylidenepyridoxine gives no colour reaction with 2 : 6 dichloroquinone-chloroimide in an alkaline buffer, but the characteristic blue colour for a phenol is shown if the compound is previously hydrolysed by mere dissolution in dilute acid for a few seconds. The rate of acid hydrolysis has, however, not been studied quantitatively, and the phenol test is extremely sensitive.

cyclo*Hexylidenepyridoxine*.—Pyridoxine hydrochloride (3 g.) was stirred with *cyclo*hexanone (60 ml.) containing concentrated sulphuric acid (6 ml.) for 2½ hours. After 60 hours at room temperature the solution was treated with a solution of sodium (5·15 g.) in absolute alcohol, and the solvent and excess of *cyclo*hexanone were removed by distillation. The residue was extracted with chloroform, and, after removal of chloroform, the extract was treated with anhydrous alcoholic hydrogen chloride which yielded cyclo*hexylidenepyridoxine hydrochloride*, colourless crystals (from alcohol), m. p. 224—225° (decomp.) (Found: C, 59·0; H, 6·8; N, 5·4. $C_{14}H_{20}O_3NCl$ requires C, 58·8; H, 7·0; N, 4·9%).

5-Chloromethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine Hydrochloride.—The alcoholic mother-liquors remaining from the isolation of pyridoxine hydrochloride after nitrous acid treatment of 4 : 5-bisaminomethyl-3-hydroxy-2-methylpyridine (preceding paper) were concentrated under reduced pressure and treated with anhydrous ether, which precipitated a hydrochloride, melting range 150—160°. Repeated crystallisation from absolute alcohol yielded cream-coloured flat needles, m. p. 170—171° (decomp.) (Found: C, 43·1; H, 5·2; N, 6·0; Cl, 31·3. $C_8H_{11}O_2NCl_2$ requires C, 42·9; H, 4·9; N, 6·25; Cl, 31·7%).

A solution of this compound (2·24 g.) in dry acetone (25 ml.) containing sulphuric acid (2·5 g.) was kept at room temperature for 24 hours after being warmed for a short time at 40°. It was filtered and most of the acetone removed under reduced pressure. The concentrate was poured into chloroform and an excess of sodium hydrogen carbonate (5 g.). Chloroform-extraction was repeated three times. The extract was dried and evaporated, and the residual oil treated in a small amount of ethanol with anhydrous ethereal hydrogen chloride. The iso*propylidene* derivative *hydrochloride* crystallised and was collected, washed with acetone, and dried (1·2 g.). Recrystallised from alcohol–ether, it formed colourless fine needles, m. p. 190—191° (decomp.) (Found: N, 5·55. $C_{11}H_{15}O_2NCl_2$ requires N, 5·3%), readily soluble in water, the solution giving a negative 2 : 6-dichloroquinone-chloroimide test. Liberation of the phenol group by brief heating with dilute acid is shown by the rapid appearance of the characteristic blue colour reaction with the above reagent.

The compound was identical in m. p. and mixed m. p. with material prepared as follows, from *iso*propylidenepyridoxine. The latter was gently refluxed with excess of thionyl chloride under anhydrous conditions. After volatilisation of excess of reagent, the residue was crystallised from alcohol–anhydrous ether, forming colourless needles of the *iso*propylidene derivative hydrochloride, m. p. 190° (decomp.).

5-Diethylaminomethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine Hydrochloride.—A mixture of the 5-chloromethyl compound (2·24 g., 0·01 mole) and diethylamine (7 g.) was heated at 60° in a sealed tube for 16 hours. After addition of N-sodium hydroxide (20 ml.) the mixture

was evaporated to dryness and the oily residue extracted with boiling absolute alcohol and filtered from sodium chloride. The alcohol was removed under reduced pressure and the residual brown viscous oil (2·45 g.) dissolved in water (25 ml.) and made slightly acid with dilute hydrochloric acid. Addition of excess of picric acid solution precipitated the *dipicrate* (2·4 g.) which, crystallised from acetic acid, had m. p. *ca.* 174° (Found: N, 16·55. $C_{24}H_{36}O_{16}N_8$ requires N, 16·4%). This was treated with dilute hydrochloric acid and exhaustively extracted with ether. The remaining aqueous solution was evaporated to dryness under reduced pressure, and the residue, on crystallisation from methanol–ether, yielded *5-diethylaminomethyl-3-hydroxy-4-hydroxymethyl-2-methylpyridine hydrochloride*, decomp. 212—214° (Found: N, 9·2; Cl, 24·6. $C_{12}H_{22}O_2N_2Cl_2$ requires N, 9·4; Cl, 23·9%).

3-Hydroxy-4-hydroxymethyl-2-methylpyridine-5-carboxylic Lactone.—A solution of *iso*propylidenepyridoxine (3 g.) in water (600 ml.) was stirred at room temperature while a solution of potassium permanganate (3·02 g.) in water (120 ml.) was run in during 3½ hours. Stirring was continued for a further 1½ hours, and manganese dioxide was removed and washed with water in the centrifuge. The combined supernatant liquid was just acidified to litmus with 2N-hydrochloric acid. A further precipitation of manganese dioxide was removed and the clear solution evaporated to dryness under reduced pressure. The residue was heated on a steam-bath for 1 hour with water (10 ml.) and concentrated hydrochloric acid (5 ml.) to effect hydrolysis and lactonisation. After evaporation to dryness the residue was redissolved in water and the product precipitated by addition of sodium acetate. Acetic acid was removed under reduced pressure and the solid collected after cooling, washed with a little cold water, and dried [0·8 g.; m. p. 270—280° (decomp.)]. The m. p. of material recrystallised from alcohol varied somewhat with heating conditions, the same specimen giving values from 273° (decomp.) (after softening from 270°) to 282—283° (Found: C, 58·1, 58·2; H, 4·4, 4·2; N, 9·0, 8·85. Calc. for $C_8H_7O_3N$: C, 58·2; H, 4·2; N, 8·5%).

We are indebted to Miss J. Ward and Mr. M. W. Parkes for the microbiological and pharmacological tests respectively, and to Drs. J. Baddiley and A. P. Mathias for making available the manuscript of their paper.

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840. *Synthetical Experiments in the B Group of Vitamins. Part VI.* Synthesis of the Pyridoxine Analogue, 2-Benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine.*

By A. COHEN and J. A. SILK.

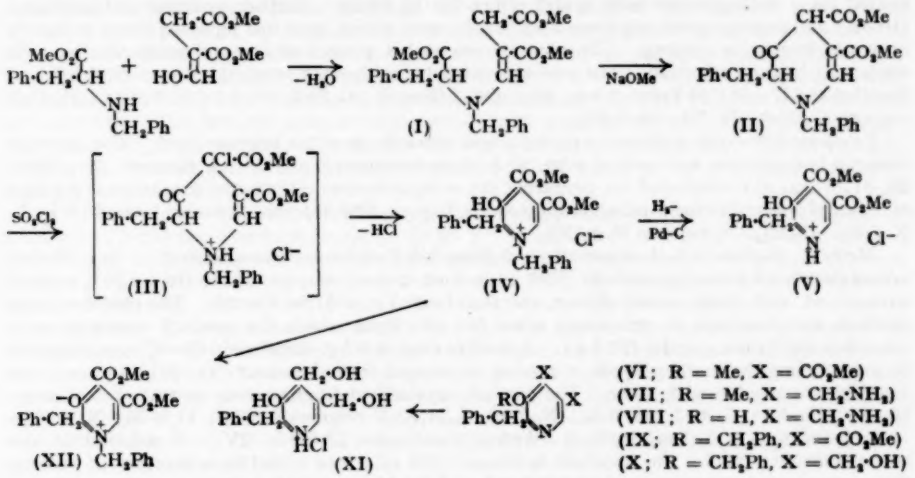
2-Benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine hydrochloride, a 2-benzyl analogue of pyridoxine, has been synthesised. It possesses little or no pyridoxine-like or antipyridoxine activity in microbiological tests.

ALTHOUGH a considerable number of compounds structurally related to pyridoxine have been examined for vitamin B_6 activity (for references see Williams, Eakin, Beerstecher, and Shive, "Biochemistry of B Vitamins," Reinhold, New York, 1950, p. 652), there has been comparatively little study of analogues in which the 2-substituent of the pyridine nucleus has been varied. The 2-ethyl analogue synthesised by Harris and Wilson (*J. Amer. Chem. Soc.*, 1941, **63**, 2526) showed less than 2% of pyridoxine activity in rats depleted of vitamin B_6. A synthesis of pyridoxine from an alanine derivative described in Part IV (*J.*, 1952, 4374) offers a flexible method of providing analogues with different 2-substituents, and 2-benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine hydrochloride (XI) has now been synthesised from a phenylalanine derivative. The synthesis of other analogues by this route has been undertaken by Dr. F. B. Kipping and his colleagues at Cambridge.

By the methods described in Part IV (*loc. cit.*), methyl α-benzylamino-β-phenylpropionate was condensed with methyl α-formylsuccinate, to yield methyl *N*-benzyl-*N*-

* Part V, preceding paper.

(1-carbomethoxy-2-phenylethyl)aminomethylenesuccinate (I) which was cyclised by sodium methoxide (cf. II). The crude cyclic keto-ester was directly treated with sulphuryl chloride, furnishing, presumably, through the intermediate chloroketone hydrochloride (III), the fully aromatic 1 : 2-dibenzyl-4 : 5-dicarbomethoxy-3-hydroxypyridinium chloride (IV). In spite of its quaternary salt character this compound is hydrolysed to such an extent in water, that the corresponding sparingly soluble phenol-betaine (XII) may be readily



isolated. The strength of the pyridinium base is no doubt considerably weakened by the neighbouring electron-attracting phenyl groups.

Hydrogenolysis of the *N*-benzyl group of (IV) led to methyl 2-benzyl-3-hydroxypyridine-4 : 5-dicarboxylate hydrochloride (V), the free base of which was methylated by diazomethane to methyl 2-benzyl-3-methoxypyridine-4 : 5-dicarboxylate (VI). This was converted by standard procedures *via* the diamide and dinitrile to the 4 : 5-bisaminomethyl compound (VII) which was demethylated by concentrated hydrobromic acid to 4 : 5-bisaminomethyl-2-benzyl-3-hydroxypyridine trihydrobromide (VIII). Exchange of hydrobromide for hydrochloride and then nitrous acid treatment furnished the desired 2-benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine hydrochloride (XI).

Alternatively, benzylation of the phenolic group of (V) with benzyldimethylphenylammonium hydroxide yielded methyl 2-benzyl-3-benzyloxypyridine-4 : 5-dicarboxylate (IX) which could be reduced by lithium aluminium hydride to 2-benzyl-3-benzyloxy-4 : 5-bishydroxymethylpyridine (X). Hydrogenolysis of the 3-benzyloxy-group then led to the 2-benzyl analogue (XI), a more convenient procedure than that outlined above.

Microbiological tests of the 2-benzyl analogue of pyridoxine by Miss J. Ward, B.Sc., of these laboratories, show that the compound only possesses slightly inhibitory action on *Staphylococcus aureus* and *B. coli* at a dilution of 1 : 2000. When tested alone it has no pyridoxine activity for *Neurospora sitophila* but, in the presence of 0·5 μg. of pyridoxine, 0·5 mg. of the analogue had a growth-promoting effect equivalent to that of 0·6 μg. of pyridoxine, indicating " activity " five thousand times less than that of pyridoxine. In conjunction with the results of animal tests on the ethyl homologue (Harris and Wilson, *loc. cit.*), it therefore appears that some degree of specificity is associated with the 2-methyl group for pyridoxine activity. This is rather surprising since the coenzyme function of pyridoxine and its congeners involves only the 4- and 5-hydroxymethyl groups, the former by its conversion into an aldehyde (pyridoxal) or aminomethyl (pyridoxamine) group, and the latter in esterification with phosphoric acid, as in pyridoxal phosphate. The influence of different 2-substituents on the nitrogen atom and the 3-hydroxy-group may contribute to the biological selectivity.

Experimental

α-Benzylamino-β-phenylpropionic acid was prepared in 77% yield by the method of Fischer and von Mechel (*Ber.*, **1916**, **49**, 1355) from benzylamine and α-bromo-β-phenylpropionic acid (Marvel, *Org. Synth.*, **21**, 100).

Methyl α-Benzylamino-β-phenylpropionate.—α-Benzylamino-β-phenylpropionic acid (39 g.) was partly dissolved in concentrated sulphuric acid (50 ml.), mixed with methanol (50 ml.), and heated on a boiling-water bath under reflux for 2½ hours. Further quantities of methanol (10 ml.) and concentrated sulphuric acid (2 ml.) were added, and this repeated twice at hourly intervals during the heating. The mixture was cooled, poured on ice, and made alkaline with sodium hydrogen carbonate. The *ester* was extracted with ether, washed with water, dried, and distilled at 137—141°/0·3 mm. (yield, 32 g., 68%) (Found: C, 75·6; H, 7·3; N, 5·5. $C_{17}H_{19}O_2N$ requires C, 75·9; H, 7·1; N, 5·2%).

Esterification with methanol and hydrogen chloride gave an inferior yield. The reaction between benzylamine and methyl α-bromo-β-phenylpropionate at 100° (cf. Bischoff, *Ber.*, 1897, **30**, 3170) was also employed for preparing the α-benzylamino-ester but a considerable amount of *N-benzyl α-benzylamino-β-phenylpropionamide*, b. p. *ca.* 220°/0·4 mm., was also formed (Found: N, 7·95. $C_{23}H_{24}ON_2$ requires N, 8·15%).

Methyl N-Benzyl-N-(1-carbomethoxy-2-phenylethyl)aminomethylenesuccinate (I).—Methyl α-benzylamino-β-phenylpropionate (23·9 g.) and methyl α-formylsuccinate (18 g., 20% excess) were mixed, with development of heat, and then heated at 100° for 3 hours. The cooled viscous mixture was dissolved in anhydrous ether (80 ml.) from which the product separated as a colourless crystalline powder (23·5 g.). A further crop of 6·1 g. (total yield 78·4%) was obtained by evaporating the mother-liquor, removing unchanged formylsuccinate at 130°/oil-pump, and digesting the residue with ether. The *product*, crystallised from aqueous methanol, had m. p. 85—86° (Found: C, 67·7; H, 6·55; N, 2·9. $C_{24}H_{27}O_6N$ requires C, 67·8; H, 6·35; N, 3·3%).

1 : 2-Dibenzyl-4 : 5-dicarbomethoxy-3-hydroxypyridinium Chloride (IV).—A solution of the above itaconate (24·6 g.) in absolute methanol (130 ml.) was added to a solution of sodium (2·0 g.) in absolute methanol (50 ml.) and refluxed for 1½ hours under nitrogen. The methanol was removed under reduced pressure and the residue dissolved in benzene and poured into a mixture of ice and sufficient acetic acid containing a little dilute sulphuric acid to render the mixture just acid to litmus. The aqueous portion was separated and re-extracted twice with benzene. The combined benzene extracts were washed with water, sodium hydrogen carbonate, and water again, and dried (Na_2SO_4). Evaporation of part of the solvent completed the drying, and the benzene solution was treated, with cooling, with sulphuryl chloride (4·0 ml.) added dropwise until no further precipitation of brown oil occurred. This heavy oil was allowed to settle, separated, and warmed at 40—45° under reduced pressure (water-pump). The residual frothy gum was dissolved in warm dry acetone (15 ml.), and a little dry ether added. On cooling, *1 : 2-dibenzyl-4 : 5-dicarbomethoxy-3-hydroxypyridinium chloride*, m. p. 135—137° (decomp.), separated (19·4 g., 79%) (Found, on material recrystallised from methanol–ether: C, 64·5; H, 5·15; N, 3·45. $C_{23}H_{22}O_5NCl$ requires C, 64·5; H, 5·15; N, 3·3%). It gives a deep red colour with ferric chloride; its aqueous solution is acid to Congo-red, and deposits the corresponging *phenol-betaine* (XII), as a pale yellow powder, which, on being dried and recrystallised from methanol–ether, has m. p. 168° (decomp.) (Found: C, 69·6; H, 5·5. $C_{23}H_{21}O_5N$ requires C, 70·5; H, 5·35%).

Methyl 2-Benzyl-3-hydroxypyridine-4 : 5-dicarboxylate Hydrochloride (V).—A solution of the above pyridinium salt (17·7 g.) in methanol (50 ml.) was shaken in hydrogen with 10% palladised charcoal (1·9 g.). Absorption was rapid and almost quantitative (940 ml.). The filtered solution was evaporated to dryness under reduced pressure and the residue digested with dry ether and warmed with a little dry acetone which induced crystallisation (13·3 g., 95%). Crystallisation from methanol–ether gave colourless plates of *methyl 2-benzyl-3-hydroxypyridine-4 : 5-dicarboxylate hydrochloride*, m. p. 148—150° (decomp.) (Found: C, 57·3; H, 4·8; N, 4·2; Cl, 10·2. $C_{16}H_{16}O_5NCl$ requires C, 56·9; H, 4·7; N, 4·15; Cl, 10·5%). Hydrolysis with 10% sodium hydroxide solution furnished the *4 : 5-dicarboxylic acid*, m. p. 241° (Found: C, 61·2; H, 4·2; N, 5·5. $C_{14}H_{11}O_5N$ requires C, 61·2; H, 4·0; N, 5·15%).

2-Benzyl-3-methoxypyridine-4 : 5-dicarboxyamide.—The above hydrochloride was converted into the free base by concentrated aqueous sodium hydrogen carbonate or acetate. Dried crude methyl 2-benzyl-3-hydroxypyridine-4 : 5-dicarboxylate so obtained (7·5 g.) was added portionwise to ethereal diazomethane (80 ml.) [from nitrosomethylurethane (12·5 ml.)]. After a few days at room temperature, excess of diazomethane and the solvent were removed. The

residual oily crude methyl 2-benzyl-3-methoxypyridine-4 : 5-dicarboxylate (VI) (negative test for phenol with dichloroquinone-imide reagent) was kept in liquid ammonia (25 ml.) in a sealed tube for 40 hours. Evaporation then left a yellow solid which was triturated with cold methanol, filtered off, and dried (5·0 g., 70%). *2-Benzyl-3-methoxypyridine-4 : 5-dicarboxyamide* crystallised from methanol in colourless plates, m. p. 194° (decomp. to imide and ammonia) (Found : C, 63·0; H, 5·2; N, 14·4; OMe, 11·1. $C_{15}H_{15}O_3N_3$ requires C, 63·1; H, 5·3; N, 14·7; OMe, 10·9%).

2-Benzyl-4 : 5-dicyano-3-methoxypyridine.—A cold suspension of the diamide (5·05 g.) in dry pyridine (30 ml.) and dry benzene (12 ml.) was stirred and treated with phosphoryl chloride (2·5 ml.) and warmed gradually; the temperature of the mixture suddenly rose spontaneously to about 40°. The mixture was stirred at about 65° for 1 hour, cooled, and decomposed with ice-water. The whole was evaporated to a small volume under reduced pressure and extracted with benzene. The benzene solution was washed with aqueous sodium hydrogen carbonate, dried, and freed from solvent. The residue was best purified by sublimation in a high vacuum, yielding the *dinitrile* as a white crystalline solid, m. p. 64° (3·23 g., 73%) (Found : N, 16·6. $C_{15}H_{11}ON_3$ requires N, 16·9%).

4 : 5-Bisaminomethyl-2-benzyl-3-methoxypyridine Trihydrochloride (cf. VII).—A solution of 2-benzyl-4 : 5-dicyano-3-methoxypyridine (3·23 g.) in methanol (95 ml.) and concentrated hydrochloric acid (5 ml.) was added in 3-ml. portions to a suspension of palladised charcoal (3·8 g.; cf. Alexander and Cope, *J. Amer. Chem. Soc.*, 1944, **66**, 888, note 7), and suspended in methanol (25 ml.) and water (5 ml.), the whole being shaken in hydrogen at approx. 1 atmosphere. Hydrogenation was complete in about 6 hours. The catalyst was filtered off, and the filtrate evaporated to dryness under reduced pressure. The residue was digested with absolute alcohol (5 ml.), filtered, and washed with alcohol (yield 3·35 g.); a further 0·5 g. was obtained by addition of dry ether to the alcoholic liquor. Recrystallisation from methanol–ether yielded *4 : 5-bisaminomethyl-2-benzyl-3-methoxypyridine trihydrochloride monohydrate*, m. p. 193° (Found : C, 47·3; H, 6·2; N, 11·0; Cl, 27·2. $C_{15}H_{22}ON_3Cl_3,H_2O$ requires C, 46·9; H, 6·2; N, 10·9; Cl, 27·7%).

4 : 5-Bisaminomethyl-2-benzyl-3-hydroxypyridine Trihydrobromide (cf. VIII).—A solution of the above methoxy-diamine trihydrochloride (2·25 g.) in hydrobromic acid (*d* 1·5; 20 ml.) was boiled under reflux for 2 hours. The solution was slightly diluted with water, treated with charcoal, and filtered hot. The filtrate was evaporated under reduced pressure until much crystalline product had separated. After cooling in ice, this was filtered off and washed with acetone, yielding 2·55 g. of the trihydrobromide which crystallised from methanol–ether as a *dihydrate*, m. p. 255—260° followed by decomposition (Found : Br, 46·2. $C_{14}H_{20}ON_3Br_3,2H_2O$ requires Br, 46·0%).

Methyl 2-Benzyl-3-benzyloxypyridine-4 : 5-dicarboxylate (IX).—A cold solution of methyl 2-benzyl-3-hydroxypyridine-4 : 5-dicarboxylate hydrochloride (12·3 g.) in absolute methanol (25 ml.) was treated with a solution of sodium (1·7 g.; 2 equivs.) in absolute methanol (25 ml.). A solution of benzyldimethylphenylammonium chloride (9 g.) in absolute methanol (20 ml.) was added and the mixture run into boiling xylene (100 ml.) stirred under nitrogen in an apparatus arranged for the distillation of the methanol and some of the xylene. Stirring was continued for 2½ hours while the mixture was heated in an oil-bath at about 150°. The sodium chloride was filtered off from the xylene solution which was cooled and washed with 0·5N-sodium hydroxide at 0° to remove any phenolic material, washed with water and dried (Na_2SO_4). The solvent and dimethylaniline were removed under reduced pressure, and the residual oil digested with warm light petroleum (b. p. 40—60°) which induced crystallisation. The dried product (10 g.) had m. p. 78° after recrystallisation from concentrated methanolic solution in colourless prisms (Found : C, 70·8; H, 5·55. $C_{23}H_{21}O_5N$ requires C, 70·6; H, 5·37%).

2-Benzyl-3-benzyloxy-4 : 5-bishydroxymethylpyridine Hydrochloride (cf. X).—Lithium aluminium hydride (0·6 g.) was stirred with sodium-dried ether (50 ml.) in nitrogen. A solution of methyl 2-benzyl-3-benzyloxypyridine-4 : 5-dicarboxylate (4·5 g.) in dry ether (75 ml.) was slowly added at 0°. The yellow precipitate which formed was stirred for 1½ hours, and decomposed by 5N-hydrochloric acid (18 ml.) with ice-cooling. The insoluble hydrochloride remaining was filtered off, washed with a little cold water, and dried *in vacuo* (yield 3·8 g., 88·5%; m. p. 170°). Recrystallisation from methanol–ether gave colourless needles of *2-benzyl-3-benzyloxy-4 : 5-bishydroxymethylpyridine hydrochloride*, m. p. 179—180° (Found : C, 68·0; H, 6·0; N, 4·1. $C_{21}H_{22}O_3NCl$ requires C, 67·8; H, 5·9; N, 3·8%).

2-Benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine Hydrochloride (XI).—(*a*) The 3-benzyloxy-derivative (1·86 g. of hydrochloride) and 20% palladised charcoal (0·6 g.) in alcohol (70 ml.)

and water (11 ml.) were shaken in hydrogen until the rapid uptake was complete. After filtration, the solution was evaporated to dryness under reduced pressure and the residue recrystallised from alcohol, yielding *2-benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine hydrochloride* as colourless feathery needles, m. p. 202° (decomp.) (Found: C, 59·8; H, 5·8; N, 5·1; Cl, 12·44. $C_{14}H_{16}O_3NCl$ requires C, 59·7; H, 5·7; N, 5·0; Cl, 12·6%).

(*b*) A solution of 2-benzyl-3-hydroxy-4 : 5-bisaminomethylpyridine trihydrobromide (1·0 g.) in water (8 ml.) was stirred with freshly prepared silver chloride (from 2·2 g. of silver nitrate) for 45 minutes on the hot-water bath, to convert the hydrobromide into hydrochloride. The mixture was filtered, and the silver halide washed with a little warm water. The solution was further clarified with the aid of kieselguhr, and mixed with 2N-hydrochloric acid (16 ml.). The whole was treated with sodium nitrite solution (10%; 3·4 ml.) on the water-bath for 30 minutes. The solution was evaporated to dryness under reduced pressure (bath *ca.* 50—60°) and the dry residue extracted with boiling absolute alcohol. Concentration of the filtered extract led to crystallisation of 2-benzyl-3-hydroxy-4 : 5-bishydroxymethylpyridine hydrochloride (0·235 g., 41%), identical with that described above.

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841. *High-polymer Solutions. Part II.* The Determination of Number-average Molecular Weights from Measurements of Osmotic Pressure.*

By ESMÉ DUCKER, E. C. FIELLER, H. T. HOOKWAY, and R. TOWNSEND.

Careful measurements of the osmotic pressures of benzene solutions of polymethyl methacrylate and of polyvinyl thiolacetate have been statistically analysed to find the best equation for extrapolation of the reduced osmotic pressure–concentration relation to infinite dilution. A similar analysis of results obtained with solutions of polystyrene in benzene, toluene, and butanone is also reported. In the concentration range studied there is no advantage in expressing the results by other than the rectilinear relation $\pi/C = a + bC$ (π = osmotic pressure, C = concentration, a and b = constants).

THE limiting value of π/C at infinite dilution may be shown to be a true measure of the molecular weight of a polymer, independent of its size or shape or the nature of the solvent used. Thus the accuracy of determination of the molecular weight of a polymer depends to a considerable extent on the nature and reliability of the extrapolation of experimental measurements to infinite dilution. A number of authors (see, *e.g.*, McMillan and Mayer, *J. Chem. Phys.*, 1945, **13**, 276; Zimm, *ibid.*, 1946, **14**, 164) have suggested that the concentration dependence of osmotic pressure may be expressed as a convergent series

$$\pi = RT(aC + bC^2 + dC^3 + \cdots) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

Recently Fox, Flory, and Bueche (*J. Amer. Chem. Soc.*, 1951, **73**, 285) have used published osmotic data in support of a theoretically derived equation which has been expressed in equation (iv) (below) as a restricted form of equation (i).

In Part I * of this series, Hookway and Townsend reported a series of measurements of osmotic pressure with a number of different polymers. In order so far as possible to render the interpretation of these and other results truly objective, the results have been statistically analysed to determine whether they best fit equations of the form (ii), (iii), or (iv).

$$\pi/C = a + bC \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

$$\pi/C = a + bC + dC^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(iii)}$$

$$\pi/C = a_1[1 + b_1C + \tfrac{2}{3}b_1^2C^2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(iv)}$$

* Part I, *J.*, 1952, 3190.

Results.—Measurements of osmotic pressure were made by means of the membranes and apparatus described in Part I (*loc. cit.*). The results presented in Table 1 for polymethyl methacrylate (D), polyvinyl thiolacetate (E), and polystyrenes (A) and (B) are based on data given in Tables 3 and 4 of Part I. In Table 2 the osmotic pressures of solutions of polystyrene in various solvents at 31·5° are recorded; C_1 = polymer concentration in g./100 c.c. of solvent; C_2 = polymer concentration in g./100 c.c. of solution; π_2 = osmotic pressure based on concentration C_2; π_3 = osmotic pressure corrected for depth of immersion of osmometer (see Part I for details).

In the calculations underlying Tables 1 and 3, equations (ii) and (iii) were rewritten in the forms

$$\pi = aC + bC^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (v)$$

$$\pi = aC + bC^2 + dC^3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (vi)$$

and fitted to the observed data by the ordinary least-squares technique. Equation (iv) was rewritten as

$$\pi = a_1C + a_1b_1C^2 + \tfrac{3}{4}a_1b_1^2C^3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (vii)$$

leading to least-squares estimates of a_1 and b_1 satisfying the pair of equations

$$\Sigma\{(C + b_1C^2 + \tfrac{3}{4}b_1^2C^3)(\pi - a_1C - a_1b_1C^2 - \tfrac{3}{4}a_1b_1^2C^3)\} = 0 \quad . \quad . \quad (viii$$

$$\Sigma\{(C^2 + \tfrac{4}{3}b_1C^3)(\pi - a_1C - a_1b_1C^2 - \tfrac{3}{4}a_1b_1^2C^3)\} = 0 \quad . \quad . \quad . \quad . \quad (ix)$$

where Σ denotes a summation over all pairs of observations (π, C). Equations (viii) and (ix) are equivalent to the pair (x) and (xi):

$$a_1\Sigma\{(C^2 + \tfrac{4}{3}b_1C^3)(C + b_1C^2 + \tfrac{3}{4}b_1^2C^3)\} = \Sigma\{\pi(C^2 + \tfrac{4}{3}b_1C^3)\} \quad . \quad . \quad . \quad (x)$$

$$a_1\Sigma\{(2C + b_1C^2)(C + b_1C^2 + \tfrac{3}{4}b_1^2C^3)\} = \Sigma\{\pi(2C + b_1C^2)\} \quad . \quad . \quad . \quad (xi)$$

and a_1 may be eliminated from these to yield a quartic equation which b_1 must satisfy. Tables 1 and 3 give for each system the appropriate root of this quartic and the corresponding value of

TABLE 1.

Polymer	Equation	a	b	d	Mean-squared deviation, $\times 10^6$
D	ii	1·8394 ± 0·0032	0·9334 ± 0·0045		1·486
	iii	1·8407 ± 0·0086	0·9282 ± 0·0315	0·0043 ± 0·0260	1·844
	iv	1·8929 ± 0·0093	0·3826 ± 0·0066		17·053
E	ii	2·5790 ± 0·0027	1·1338 ± 0·0050		0·535
	iii	2·5871 ± 0·0040	1·0908 ± 0·0195	0·0481 ± 0·0216	0·182
	iv	2·6153 ± 0·0055	0·3605 ± 0·0037		2·786
A	ii	16·3068 ± 0·0070	2·2557 ± 0·0280		0·546
	iii	16·2908 ± 0·0182	2·4346 ± 0·1873	−0·4341 ± 0·4487	0·634
B	ii	6·1066 ± 0·0133	0·9894 ± 0·0341		6·188
	iii	6·1610 ± 0·0198	0·6160 ± 0·1281	0·5574 ± 0·1894	1·732

TABLE 2.

Solvent: benzene.

C_1, g./100 c.c.	C_2, g./100 c.c.	π_1, g./cm.²	π_2, g./cm.²	π_3, g./cm.²	C_1, g./100 c.c.	C_2, g./100 c.c.	π_1, g./cm.²	π_2, g./cm.²	π_3, g./cm.²
0·0861	0·0861	0·108	0·108	0·109	0·4303	0·4307	0·681	0·682	0·687
0·1437	0·1437	0·188	0·188	0·190	0·5767	0·5776	0·996	0·997	1·003
0·2511	0·2152	0·294	0·295	0·297	0·8665	0·8682	1·741	1·744	1·753
0·2881	0·2883	0·417	0·417	0·420					

Solvent: toluene.

C_2, g./100 c.c.	π_2, g./cm.²	π_3, g./cm.²	C_2, g./100 c.c.	π_2, g./cm.²	π_3, g./cm.²	C_2, g./100 c.c.	π_2, g./cm.²	π_3, g./cm.²
0·0858	0·114	0·115	0·2851	0·487	0·490	0·5985	1·372	1·379
0·1424	0·205	0·207	0·4247	0·836	0·841	0·8546	2·371	2·381
0·2134	0·335	0·337						

Solvent: butanone.

0·0789	0·098	0·099	0·2640	0·369	0·373	0·5918	1·000	1·008
0·1314	0·168	0·170	0·3943	0·595	0·601	0·7897	1·473	1·484
0·1971	0·265	0·268						

a_1 as determined by (x) or (xi). Convenient expressions for the sampling variances of a_1 and b_1 were obtained, as may always be done for maximum likelihood estimates (Kendall, " Advanced Theory of Statistics," 1946, Vol. II, Charles Griffin & Co. Ltd.), from the Hessian of the sum of squared residuals

$$\Sigma(\pi - a_1C - a_1b_1C^2 - \tfrac{2}{3}a_1b_1^2C^3)^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(xii)}$$

The values of a, b, and d entered in Tables 1 and 3 are given in each case in the form estimate ± standard error. The final column in these tables gives the mean-squared deviation of the observed values of π from those calculated from the fitted curve. These entries were computed by dividing the sum of squared deviations by the appropriate degrees of freedom [2 less than the number of observations in the case of equations (v) and (vii); 3 less in the case of equation (vi)].

TABLE 3.

Solvent	π, C	Equation	a	b	d	Mean-squared deviation, $\times 10^6$
Benzene	π_1, C_1	ii	1·1637 ± 0·0023	0·9759 ± 0·0032		0·741
		iii	1·1634 ± 0·0061	0·9771 ± 0·0225	−0·0010 ± 0·0187	0·927
		iv	1·2374 ± 0·0122	0·5557 ± 0·0132		31·523
	π_2, C_2	ii	1·1651 ± 0·0012	0·9716 ± 0·0017		0·221
		iii	1·1667 ± 0·0032	0·9655 ± 0·0119	0·0051 ± 0·0099	0·262
		iv	1·2385 ± 0·0117	0·5532 ± 0·0127		29·292
	π_3, C_2	ii	1·1764 ± 0·0019	0·9705 ± 0·0026		0·494
		iii	1·1781 ± 0·0049	0·9639 ± 0·0180	0·0055 ± 0·0149	0·596
		iv	1·2493 ± 0·0117	0·5491 ± 0·0125		29·064
Toluene	π_2, C_2	ii	1·1711 ± 0·0015	1·8758 ± 0·0021		0·289
		iii	1·1740 ± 0·0034	1·8639 ± 0·0128	0·0101 ± 0·0108	0·296
		iv	1·3552 ± 0·0284	0·8485 ± 0·0295		186·138
	π_3, C_2	ii	1·1821 ± 0·0017	1·8766 ± 0·0024		0·379
		iii	1·1844 ± 0·0042	1·8674 ± 0·0155	0·0079 ± 0·0131	0·435
		iv	1·3657 ± 0·0285	0·8441 ± 0·0294		186·608
Butanone	π_2, C_2	ii	1·1623 ± 0·0031	0·8901 ± 0·0047		1·072
		iii	1·1674 ± 0·0072	0·8671 ± 0·0291	0·0215 ± 0·0268	1·154
		iv	1·2167 ± 0·0093	0·5366 ± 0·0111		13·497
	π_3, C_2	ii	1·1777 ± 0·0028	0·8880 ± 0·0042		0·864
		iii	1·1840 ± 0·0060	0·8597 ± 0·0243	0·0265 ± 0·0224	0·801
		iv	1·2315 ± 0·0089	0·5306 ± 0·0105		12·303

Discussion.—The principal object of this work has been to find the best method of determining the coefficient a. In view of the hetero-disperse nature of the polymers studied, no attempt has been made to attach any physical significance to the coefficients b and d.

The close agreement between the observed and calculated values of π, in the case of equations (v) and (vi), is at once apparent from the small size of the mean-squared deviations, and is illustrated in detail for polymer E in Table 4.

TABLE 4. *Observed and calculated values of* π.

	π, g./cm.²			
C, g./100 c.c.	Obs.	Eqn. (v)	Eqn. (vi)	Eqn. (vii)
0·0866	0·232	0·2318	0·2323	0·2337
0·1454	0·399	0·3990	0·3994	0·4008
0·2165	0·612	0·6115	0·6117	0·6126
0·2892	0·841	0·8407	0·8406	0·8403
0·4332	1·329	1·3300	1·3293	1·3271
0·6481	2·148	2·1477	2·1479	2·1487

It can be seen from the values of the mean-squared deviations in Tables 1 and 3 that in no case is the unrestricted parabola [equation (iii)] significantly superior to the straight line [equation (ii)]; indeed, to discriminate between them would appear to demand more precise measurements of π than can as yet be made. The virtual agreement between equations (ii) and (iii) is indicated also by the agreement between the pairs of values of a

that they supply, and also by the relatively high values found for the standard error of the coefficients *d*. In the light of the results found, Fox, Flory, and Bueche's equation (iv) appears to have little to recommend it. It is true that, if we ignore the results of fitting (ii) and (iii), (iv) appears to explain the experimental data reasonably well; but (ii) and (iii) explain them better, and involve less complicated calculations. Cleverdon and Laker (*Chem. and Ind.*, 1951, 272) and McLeod and McIntosh (*Canadian J. Chem.*, 1951, **29**, 1104) have also made measurements which suggest that equation (iv) may not be of general application.

The data for polystyrene in three solvents presented in Tables 2 and 3 show that the values of *a* cover a range of $\pm 0{\cdot}0044$ for equation (ii) and $\pm 0{\cdot}0036$ for equation (iii). The uncertainty in molecular weight is thus about 0·75%—a satisfactory indication of the soundness of the experimental technique. Conversion of concentration units from g./100 c.c. of solvent ($\pi_1 C_1$) to g./100 c.c. of solution ($\pi_2 C_2$) does not affect the results appreciably. Similarly, correction of the osmotic pressure to allow for the depth of immersion of the osmometer ($\pi_3 C_2$) causes a change of less than 1% in the value of *a* and causes no significant change in the mean-squared deviations.

The experimental work described in this paper forms part of the programme of the Chemical Research Laboratory and this account is published by permission of the Director.

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842. *Non-saponifiable Constituents of Spanish Broom.*

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The non-saponifiable material from the concrète (extract) of Spanish broom has been investigated and the following constituents identified: a mixture of higher paraffins, a mixture of higher aliphatic alcohols, α-, β-, and δ-amyrin, lupeol, β-sitosterol, *n*-octadecane-1 : 18-diol, and *n*-hexacosane-1 : 26-diol. In addition, two unidentified alcohols have been isolated.

EXTRACTS of Spanish broom (*Spartium junceum* L.) are widely used in the French perfume industry. Little is known of their constituents (Naves and Mazuyer, "Les Parfums Naturels," Paris, 1939), the only recorded investigation being that of Sabetay and Igolen (*Ann. Chim. anal.*, 1946, **27**, 224), which was mainly concerned with the alkali-soluble fractions.

The extract available to us was obtained by digestion of the flowers with cold light petroleum followed by low-temperature removal of the solvent. The total extract (concrète) was an oily wax (0·09—0·18% of the dried flowers). Treatment of it with cold ethanol gives the alcohol-soluble "absolue" (approximately 40% of the concrète) and an insoluble wax.

The non-saponifiable matter from the broom wax is only partly soluble in cold ether. The ether-insoluble fraction was separated by chromatography into a saturated paraffin and a saturated alcohol. Chibnall, Piper, Pollard, Williams, and Sahai (*Biochem. J.*, 1934, **28**, 2189) have shown that the higher paraffins present in plant waxes are usually inseparable mixtures of straight-chain hydrocarbons which contain an odd number of carbon atoms and that naturally occurring higher alcohols are usually inseparable mixtures of homologues each containing an even number of carbon atoms. Consideration of the physical and analytical data suggests that the broom-wax paraffin is a mixture containing approximately 60% of *n*-nonacosane and 40% of *n*-hentriacontane. The broom-wax alcoholic fraction is probably a mixture of alcohols with a mean chain-length of C_{24}.

The ether-soluble fraction from broom wax was separated by chromatography into a mixture of paraffins, a mixture of alcohols similar to that obtained from the ether-insoluble fraction, a mixture of triterpenoid alcohols, from which a small amount of β-amyrin was isolated, and β-sitosterol.

The broom absolue contains a high proportion (46%) of free fatty acids. After removal of these the neutral fraction was hydrolysed, and the non-saponifiable material, which constituted approximately 20% of the absolue, was separated by chromatography on alumina. Elution of the chromatogram with benzene gave an alcohol, $C_{22}H_{46}O$ or $C_{22}H_{44}O$, m. p. 65—66°, $\alpha = 0°$, which is saturated to tetranitromethane and has no selective absorption of high intensity above 2200 Å. Since it contains one active hydrogen atom yet fails to afford acyl derivatives, and was recovered unchanged after attempted oxidation, it is probably a tertiary alcohol.

Elution of the chromatogram with benzene–ethanol gave a mixture of alcohols, chromatography of the benzoates from which gave a mixture of α- and β-amyrin benzoates, separated by crystallisation; a second benzoate fraction, which was not readily purified, was converted into the corresponding acetate which after chromatography was identified as δ-amyrin acetate [olean-13(18)-en-2"β"-yl acetate]. δ-Amyrin has not previously been isolated directly from natural sources so far as we are aware; it has been prepared from β-amyrin (Ruzicka and Jeger, *Helv. Chim. Acta*, 1941, **24**, 1236; Ruzicka, Jeger, and Norymberski, *ibid.*, 1942, **25**, 457), from lupenyl acetate by acid isomerisation, and also by a similar isomerisation of β-amyrenone followed by reduction of the carbonyl group (Ames, Halsall, and Jones, *J.*, 1951, 450). Since the last two methods require strongly acidic conditions, it is unlikely that the δ-amyrin isolated from broom has been produced from β-amyrin or from lupeol during the isolation procedure. A third benzoate fraction from the chromatogram was identified as lupenyl benzoate.

Continued elution of the original chromatogram with benzene–ethanol gave a fraction separated by crystallisation into a C_{24}-alcohol mixture and an alcohol, $C_{16}H_{32}O$. The latter contains one active hydrogen (Zerewitinoff) and its infra-red absorption spectrum shows bands at 3214 and 1064 cm.$^{-1}$. The acetate of the alcohol could not be obtained crystalline. The presence of one double bond was established by microhydrogenation.

The last fraction to be eluted with benzene–ethanol readily afforded β-sitosterol. The remaining material was held tenaciously by the alumina; partial separation was effected by mechanical division of the column. From the upper part of the chromatogram, *n*-octadecane-1 : 18-diol was isolated. Identity was established by comparison of the natural diol with a specimen prepared by lithium aluminium hydride reduction of ethyl *n*-octadecane-1 : 18-dioate and by oxidation of the natural diol to *n*-octadecane-1 : 18-dioic acid (cf. *Nature*, 1951, **168**, 298). From the lower part of the column, a second diol, $C_{26}H_{54}O_2$, was isolated. It was identified as *n*-hexacosane-1 : 26-diol by synthesis. Electrolysis of a mixture of sebacic acid and two molecular proportions of ethyl hydrogen sebacate gave a readily separable mixture of ethyl *n*-octadecane-1 : 18-dioate and ethyl *n*-hexacosane-1 : 26-dioate. Reduction of the last ester with lithium aluminium hydride gave *n*-hexacosane-1 : 26-diol, identical with the diol from broom.

Experimental

The alumina used for chromatography was Grade II (Brockmann). The light petroleum employed was a fraction of b. p. 60—80°, unless otherwise stated. Specific rotations were measured in chloroform (unless otherwise specified) in a 1-dm. tube at room temperature (18—20°).

Broom wax.

Paraffin and C_{24}*-Alcohol Mixtures.*—A solution of the dark brown wax (97 g.) in ethanolic potassium hydroxide (7·5%; 1150 ml.) was heated under reflux for 7 hours, then diluted with water (4 l.) and extracted with ether. On concentration and cooling, the extract deposited a waxy solid (fraction A; 53·9 g.; m. p. 58—64°). Evaporation of the ethereal mother-liquors gave a brown waxy solid (fraction B; 12·6 g.). A solution of fraction A (2·5 g.) in benzene (200 ml.) and light petroleum (100 ml.) was passed through alumina (20 × 3 cm.), and the chromatogram was developed with the same solvent mixture (1000 ml.) to give fraction (i) (2·1 g.) as a waxy solid, m. p. 62°. Continued washing with the same solvent (1800 ml.) gave fraction (ii) (0·32 g.) as a waxy solid, m. p. 75°. Crystallisation of fraction (i) from ethyl acetate gave a higher paraffin mixture as plates, m. p. 64—65° (1·6 g.) (Found: C, 85·4; H, 14·6. Calc. for $C_{29}H_{60}$: C, 85·2; H, 14·8. Calc. for $C_{31}H_{64}$: C, 85·2; H, 14·8%). Piper, Chibnall, Hopkins, Pollard, Smith, and Williams (*Biochem. J.*, 1931, **25**, 2072) record m. p. 64·8—65° for

a mixture of $C_{29}H_{60}$ (60%) and $C_{31}H_{64}$ (40%). Crystallisation of fraction (ii) from ethyl acetate gave the C_{24}-alcohol mixture (0·22 g.) as brittle rods, m. p. 75·5° (Found: C, 81·3; H, 14·0. $C_{24}H_{50}O$ requires C, 81·3; H, 14·2%). The mixture of acetates obtained by heating the alcohol under reflux with acetic anhydride separated from light petroleum (b. p. 40—60°) as plates, m. p. 59—60° (Found: C, 79·0; H, 13·2. Calc. for $C_{26}H_{52}O_2$: C, 78·7; H, 13·2%).

β-Amyrin and β-Sitosterol.—A solution of fraction B (12·1 g.) in benzene (250 ml.) and light petroleum (b. p. 40—60°; 250 ml.) was filtered through alumina (20 × 3 cm.). The column was washed with the same solvent mixture (1300, 2200, and 400 ml.) to give fractions, (i) a waxy solid (5·7 g.) m. p. 63°, (ii) a solid (3·4 g.), m. p. approx. 140°, and (iii) a sticky solid (0·15 g.). Extraction of the lower portion of the chromatogram with hot benzene–ethanol (9 : 1) yielded fraction (iv), a sticky solid (0·8 g.), m. p. approx. 130°. Crystallisation of fraction (ii) from ethyl acetate gave the C_{24}-alcohol mixture (1·2 g.) as needles, m. p. 75·5° alone or mixed with the specimen described above. Concentration of the mother-liquors from this crystallisation yielded a solid (1·65 g.), m. p. 147—169°, which gave a magenta Liebermann–Burchard colour. Part of this material (0·14 g.) was acetylated under reflux with acetic anhydride (3 ml.) for 3 hours. The product, crystallised successively from acetic acid and ethanol, yielded β-amyrin acetate (0·02 g.) as long needles, m. p. 235°, $[\alpha]_D$ +78° (*c*, 1·6 in benzene) (Found: C, 81·9; H, 11·4. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%); it did not depress the m. p. of an authentic specimen of β-amyrin acetate, m. p. 236°, $[\alpha]_D$ +79° (*c*, 1·0 in benzene). Crystallisation of fraction (iv) from methanol gave β-sitosterol as plates, m. p. 136·5°, $[\alpha]_D$ −34·4° (*c*, 0·6).

Broom absolue.

Alcohol $C_{22}H_{46}O$ *or* $C_{22}H_{44}O$.—A solution of the dark brown absolue (194 g.) in ether (1200 ml.) was extracted with potassium hydroxide solution (4%; 5 × 200 ml.), washed with water, and dried (Na_2SO_4). Removal of the solvent gave a dark brown oil (105 g.) with a raisin-like odour which was heated under reflux with ethanolic potassium hydroxide (5%; 1 l.) for 2 hours on the water-bath. The bulk of the ethanol was removed under reduced pressure, and replaced simultaneously by water (2 l.). The mixture was extracted with ether, and the solvent evaporated, to give the non-saponifiable fraction (40 g.) as a pleasant-smelling, clear red, viscous oil. A solution of this fraction (40 g.) in hot benzene (1 l.) was cooled and the solid separating (0·38 g.; later identified as *n*-octadecane-1 : 18-diol) collected. The benzene solution was filtered through alumina (35 × 6 cm.). Benzene (3·8 l.) eluted fraction 1 (yellow oil; 4·6 g.). Continued washing with benzene (6·8 l.) gave fraction 2 (brown wax; 2·6 g.). Benzene–ethanol (9·8 l.; 200 : 1) eluted fraction 3 (pale yellow solid, m. p. 140°; 10·4 g.). Washing with benzene–ethanol (8 l.; 200 : 1) yielded fraction 4 (waxy solid, m. p. 50°; 8·1 g.), and continued washing with the same solvent mixture (4 l.) gave fraction 5 (m. p. 120°; 4·1 g.). Fractions 6 (brown oil; 3·0 g.), 7 (partly crystalline; 1·1 g.), 8 (partly crystalline; 1·6 g.), and 9 (brown oil; 0·5 g.) were obtained from zones occupying 4, 10, 8, and 13 cm. respectively of the column, by extraction with boiling benzene–ethanol (3 : 1).

Crystallisation of fraction 2 from ethyl acetate and then from methanol gave the *alcohol* as clusters of needles (0·6 g.), m. p. 65—66° [Found: C, 81·4; H, 13·8; active H, 0·36%; *M* (Rast), 318. $C_{22}H_{46}O$ requires C, 80·9; H, 14·2; active H, 0·31%; *M*, 327. $C_{22}H_{44}O$ requires C, 81·4; H, 13·7%; *M*, 325].

β- and α-Amyrin Benzoates.—Fraction 3 was treated with pyridine (15 ml.) and benzoyl chloride (3·5 ml.) at 100° for 4 hours. A solution of the mixed benzoates (12 g.) (isolated in the usual manner) in light petroleum (b. p. 40—60°; 300 ml.) was filtered through alumina (5 × 30 cm.). Fraction (i) (3·2 g.; m. p. 190°) was obtained by washing the chromatogram with light petroleum–benzene (19 : 1; 2·2 l.). Continued washing with the same solvent mixture (1·3 l.) gave fraction (ii) (1·3 g.; m. p. 150°). Fraction (iii) (0·8 g.; m. p. 190°) was obtained by washing the chromatogram with a mixture of the same solvents (9 : 1; 800 ml.), and final washing with light petroleum–benzene (6 : 1; 1·2 l.) gave fraction (iv) (2·3 g.; m. p. 220°). Fractional crystallisation of fraction (i) from benzene–acetone gave β-amyrin benzoate (690 mg.) as rectangular plates, m. p. 235°, $[\alpha]_D$ +97° (*c*, 1·2), which did not depress the m. p. of an authentic specimen (Found: C, 83·8; H, 10·4. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·25%), and α-amyrin benzoate (120 mg.) as large prisms, m. p. 198°, $[\alpha]_D$ +92° (*c*, 1·1), undepressed in m. p. when mixed with an authentic specimen (Found: C, 83·3; H, 10·0%).

α-Amyrin Acetate.—Fraction (ii) was crystallised from benzene–acetone, and the crude benzoate (1·25 g.; m. p. 184°) hydrolysed with ethanolic potassium hydroxide (4%; 50 ml.) under reflux for 10 hours. The product, isolated in the usual manner, was heated with acetic anhydride (10 ml.) and pyridine (5 ml.) for 6 hours at 100°. Crystallisation of the acetate from

chloroform–methanol gave β-amyrin acetate {382 mg.; m. p. 235°; $[\alpha]_D$ +79° (*c*, 1·3)}. The mother-liquor was evaporated, the residue dissolved in light petroleum, and the solution filtered through alumina (2 × 20 cm.). Washing with the same solvent (300 ml.) eluted a fraction (112 mg.; m. p. 194—205°). Continued washing with light petroleum (800 ml.) gave a fraction which on crystallisation from chloroform–methanol gave δ-amyrin acetate (265 mg.) as hexagonal plates, m. p. 206·5—207·5°, $[\alpha]_D$ −30° (*c*, 1·3) (Found: C, 81·9; H, 10·9. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). A specimen prepared according to Ruzicka and Jeger's method (*loc. cit.*) had $[\alpha]_D$ −35°, m. p. 208·5—209·5° alone or mixed with the specimen described above. Light absorption (in ethanol): ε_{2050} 4200, ε_{2100} 6600, ε_{2150} 5000, ε_{2200} 3500, ε_{2250} 1750. These extinction coefficients are in good agreement with those for authentic δ-amyrin acetate.

Lupenyl Benzoate.—Crystallisation of fraction (iv) of the benzoate chromatogram from benzene–acetone gave lupenyl benzoate (0·7 g.) as plates, m. p. 265°, $[\alpha]_D$ +60·4° (*c*, 2·0), which did not depress the m. p. of an authentic specimen (Found: C, 83·6; H, 10·3. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·25%).

Alcohol, $C_{16}H_{33}O$.—Fraction 4 from the broom absolue chromatogram was crystallised from methanol, to yield a solid (3·5 g.; m. p. 50—56°). On slow cooling of a solution of this solid in methanol the C_{24}-alcohol mixture separated as fine needles (0·36 g.), m. p. 71—73°, undepressed when mixed with the specimen described above (Found: C, 81·4; H, 14·2. Calc. for $C_{24}H_{50}O$: C, 81·4; H, 14·1%). The mother-liquor from the C_{24}-alcohol mixture slowly deposited a second crop of fine needles which after recrystallisation from the same solvent gave the *alcohol*, $C_{16}H_{33}O$ (1·45 g.), m. p. 56—57° [Found: C, 79·7; H, 13·7; active H, 0·44%; *M* (Rast), 227. $C_{16}H_{33}O$ requires C, 79·9; H, 13·4; active H, 0·42%; *M*, 240]. The compound gave a pale yellow colour with tetranitromethane in chloroform and on microhydrogenation absorbed 0·7 mole of hydrogen. In the Liebermann–Burchard test, an intense royal-blue colour developed in the chloroform layer if care was taken to avoid mixing with the acid layer. The alcohol is optically inactive, does not absorb bromine in methanolic solution, and does not react with osmium tetroxide in ether.

β-*Sitosterol.*—Fraction 5 separated from methanol, to give β-sitosterol as large hexagonal plates, m. p. 137°, $[\alpha]_D$ −33·4° (*c*, 1·8). The m. p. was undepressed on admixture with an authentic specimen, m. p. 137°, $[\alpha]_D$ −35·6°. Acetylation with acetic anhydride afforded β-sitosteryl acetate as prisms (from ethanol), m. p. 127·5°, $[\alpha]_D$ −37·5° (*c*, 1·0). Benzoyl chloride and pyridine gave the benzoate as leaflets (from benzene–ethanol), m. p. 143—144·5°, $[\alpha]_D$ −14·4° (*c*, 1·1). The 3 : 5-dinitrobenzoate, prepared by using 3 : 5-dinitrobenzoyl chloride and pyridine, separated as pale yellow plates, m. p. 198—200°, $[\alpha]_D$ −10·1° (*c*, 0·5), from ethyl acetate–ethanol.

n-*Octadecane*-1 : 18-*diol.*—(*a*) Crystallisation of fraction 8 from methanol and then from benzene gave *n*-ocatadecane-1 : 18-diol (800 mg.) as soft plates, m. p. 98—99° (Found: C, 75·5; H, 13·2; active H, 0·6. Calc. for $C_{18}H_{38}O_2$: C, 75·5; H, 13·4; active H, 0·7%).

(*b*) A solution of ethyl *n*-octadecane-1 : 18-dioate (10 g.; Greaves, Linstead, Shephard, Thomas, and Weedon, *J.*, 1950, 3326) in dry ether (150 ml.) was added to a solution of lithium aluminium hydride (1·5 g.) in the same solvent (200 ml.). Working up in the usual manner gave *n*-octadecane-1 : 18-diol (sparingly soluble in ether) as plates (6·8 g.; m. p. 98—99°) from benzene. Chuit and Hausser (*Helv. Chim. Acta*, 1929, **12**, 850) record m. p. 98·6—99° for a specimen prepared by Bouveault–Blanc reduction of the same ester. A mixture with the natural diol had m. p. 98—99°; the infra-red spectra of specimens obtained by methods (*a*) and (*b*) were identical.

Heating the natural diol with acetic anhydride at 100° during 2 hours gave n-*octadecane*-1 : 18-*diol diacetate* which separated from methanol as needles, m. p. 59—60° (Found: C, 71·5; H, 11·5. $C_{22}H_{42}O_4$ requires C, 71·3; H, 11·4%); the m. p. was undepressed when mixed with a specimen prepared by acetylation of the synthetic diol.

Treatment of the natural diol with 3 : 5-dinitrobenzoyl chloride and pyridine at 100° during 1 hour gave n-*octadecane*-1 : 18-*diol bis*-3 : 5-*dinitrobenzoate* as yellow plates [from light petroleum (b. p. 100—120°)], m. p. 95° (Found: N, 7·8. $C_{32}H_{42}O_{12}N_4$ requires N, 8·3%); it was undepressed in m. p. on admixture with a specimen, m. p. 95°, prepared from the synthetic diol.

The natural diol (75 mg.) with chromium trioxide (200 mg.) in glacial acetic acid (5·5 ml.) gave *n*-octadecane-1 : 18-dioic acid which separated from chloroform as small prisms (30 mg.), m. p. 124—125° alone or mixed with a specimen of m. p. 125°, prepared by the hydrolysis of ethyl *n*-octadecane-1 : 18-dioate.

n-*Hexacosane*-1 : 26-*diol.*—(*a*) A solution of fraction 7 in hot methanol deposited a colourless solid (0·13 g.) on cooling. Repeated crystallisation from benzene afforded n-*hexacosane*-1 : 26-

diol as small prisms (40 mg.), m. p. 102—105° (Found : C, 78·2; H, 13·7. $C_{26}H_{54}O_2$ requires C, 78·3; H, 13·65%).

(*b*) (With H. Gibson.) A solution of sebacic acid (13·2 g.) and ethyl hydrogen sebacate (30 g.) in anhydrous methanol (120 ml.) in which sodium (0·1 g.) had been dissolved was electrolysed by the procedure described by Greaves, Linstead, Shephard, Thomas, and Weedon (*loc. cit.*). The neutral fraction (39·0 g.), obtained by extraction with chloroform, was distilled under reduced pressure. After the removal of an unsaturated fraction (b. p. up to 120°/3 × 10^{-3} mm.; 5·0 g.), ethyl *n*-octadecane-1 : 18-dioate (b. p. 124—126°/3 × 10^{-3} mm.) was collected; it separated from methanol as a microcrystalline powder (9·0 g.), m. p. 44—46°. Bowman and Mason (*J.*, 1951, 2748) record m. p. 47°. Hydrolysis of the ester with methanolic sodium hydroxide gave *n*-octadecane-1 : 18-dioic acid, m. p. 124—125° alone or mixed with an authentic specimen. The less volatile residue in the still crystallised from methanol, giving ethyl *n*-hexacosane-1 : 26-dioate (6·0 g.), m. p. 64—66° (Found : C, 74·9; H, 12·15. Calc. for $C_{30}H_{58}O_4$: C, 74·6; H, 12·1%). Fairweather (*Proc. Roy. Soc., Edinburgh*, 1926, **46**, 71) records m. p. 66° for a specimen of the ester prepared by the electrolysis of ethyl sodium *n*-tetradecane-1 : 14-dioate. Ethyl *n*-hexacosane-1 : 26-dioate (2·0 g.) was added to a solution of lithium aluminium hydride (1 g.) in dry ether (60 ml.). The mixture was treated with water and with dilute mineral acid, and the solid collected. Crystallisation from benzene gave *n*-hexacosane-1 : 26-diol (0·85 g.) as plates, m. p. 102—105°, undepressed when mixed with the diol obtained as described under (*a*) (Found : C, 78·15; H, 13·5%).

The diol with benzoyl chloride and pyridine at 100° during 1 hour gave n-*hexacosane*-1 : 26-*diol dibenzoate* as small needles, m. p. 67—70°, from methanol (Found : C, 78·9; H, 10·3. $C_{40}H_{62}O_4$ requires C, 79·15; H, 10·3%). With **3** : 5-dinitrobenzoyl chloride and pyridine at 100° during 1 hour it gave the *bis*-**3** : 5-*dinitrobenzoate* as pale yellow platelets, m. p. 91—93·5°, from ethanol (Found : N, 7·6. $C_{40}H_{58}O_{12}N_4$ requires N, 7·1%).

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843. 1 : 2-*Dihydro-2-thianaphthalene Derivatives. Part III.* Further Examples of the Conversion of* 1 : 2-*Dihydro-1-keto-2-thianaphthalenes into Indanones.*

By J. J. Brown and G. T. Newbold.

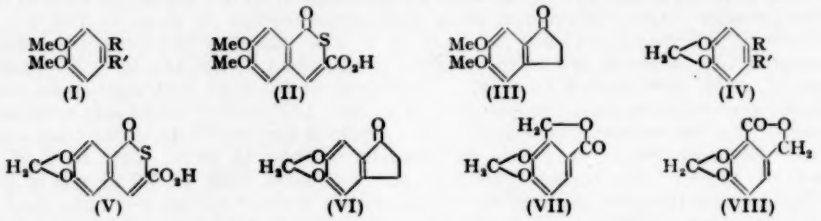
Reaction of 1 : 2-dihydro-1-keto-6 : 7-dimethoxy- and -6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid with Raney nickel give respectively 5 : 6-dimethoxy- and 5 : 6-methylenedioxy-indan-1-one. The latter compound has been obtained by the action of Raney nickel on hydrastal (6-vinylpiperonaldehyde).

Continuing the study of the conversion of 1 : 2-dihydro-1-keto-2-thianaphthalene-3-carboxylic acids into indanones (Dijksman and Newbold, *J.*, 1952, 13), we have turned to the action of Raney nickel on 1 : 2-dihydro-1-keto-6 : 7-dimethoxy- (II) and -6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid (V). These were selected because of the relationship between the expected products 5 : 6-dimethoxy- (III) and 5 : 6-methylenedioxy-indan-1-one (VI) to 4 : 5-dimethoxy-2-vinylbenzaldehyde (I; R = $CH{:}CH_2$, R′ = CHO), a degradation product of cryptopine (Perkin, *J.*, 1916, **109**, 815) and hydrastal (IV; R = $CH{:}CH_2$, R′ = CHO), obtained by degradation of hydrastine (Freund, *Ber.*, 1889, **22**, 2329) respectively.

The starting materials for the preparation of the required thianaphthalene acids were *m*-opianic acid (I; R = CO_2H, R′ = CHO) and 4 : 5-methylenedioxyphthalaldehydic acid (IV; R = CO_2H, R′ = CHO). *m*-Opianic acid has been synthesised by several

* Part II, *J.*, 1952, 13.

methods, of which none is of preparative use (Fargher and Perkin, *J.*, 1921, **119**, 1724; Perkin and Stoyle, *J.*, 1923, **123**, 3171; Chakravarti and Swaminathan, *J. Indian Chem. Soc.*, 1934, **11**, 715). *m*-Meconin, the lactone of (I; R = CO_2H, R′ = CH_2OH), is readily available, being formed, albeit in low yield, by the action of paraformaldehyde in hydrochloric acid on veratric acid (Edwards, Perkin, and Stoyle, *J.*, 1925, **127**, 195). These

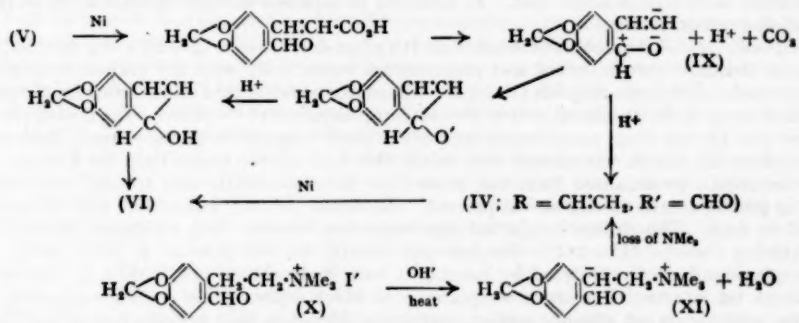


authors, however, reported that oxidation of *m*-meconin with manganese dioxide in sulphuric acid gave only traces of *m*-opianic acid (I; R = CO_2H, R′ = CHO). An alternative method of oxidation was therefore desirable and was suggested by the experience of Hirshberg, Lavie, and Bergmann (*J.*, 1951, 1030) who showed that phthalide could be smoothly converted by aid of *N*-bromosuccinimide into 3-bromophthalide, which readily gives phthalaldehydic acid when heated with water (Racine, *Annalen*, 1887, **239**, 79). We find that bromination of *m*-meconin with *N*-bromosuccinimide followed by hydrolysis without isolation of the intermediate bromo-compound gives *m*-opianic acid in 65% yield. Similar treatment of 5 : 6-methylenedioxyphthalide, the lactone of (IV; R = CO_2H, R′ = CH_2OH), readily prepared from homopiperonylic acid after Stevens (*J.*, 1927, 178; Stevens and Robertson, *ibid.*, p. 2790), gave 4 : 5-methylenedioxyphthalaldehydic acid (IV; R = CO_2H, R′ = CHO) in 72% yield. Stevens and Robertson (*loc. cit.*) reported that (IV; R = CO_2H, R′ = CHO) could not be obtained from the lactone of (IV; R = CO_2H, R′ = CH_2·OH) by oxidation with manganese dioxide or lead dioxide in sulphuric or acetic acid or by use of chromium trioxide in acetic acid. 4 : 5-Methylenedioxyphthalaldehydic acid has been prepared by Chakravarti, Swaminathan, and Venkataraman (*J. Indian Chem. Soc.*, 1940, **17**, 264) by a similar route to that described by Chakravarti and Swaminathan (*loc. cit.*) for *m*-opianic acid. An attempt was made to prepare 5 : 6-methylenedioxyphthalide by the action of paraformaldehyde in hydrochloric acid on piperonylic acid (IV; R = CO_2H, R′ = H), though Edwards, Perkin, and Stoyle (*loc. cit.*) reported that piperonylic acid on long boiling with formaldehyde and hydrochloric acid gave a small yield of an easily oxidised substance of high molecular weight. We confirmed that the bulk of piperonylic acid was recovered after the reaction, but isolated a small quantity of a compound $C_9H_6O_4$, m. p. 176—178°, having the properties of a phthalide and whose ultra-violet light absorption (see Experimental) is similar to that of 5 : 6-methylenedioxyphthalide. We believe this compound to be 4 : 5-methylenedioxyphthalide (VII). The third isomer, 6 : 7-methylenedioxyphthalide (VIII), m. p. 233—234°, has been synthesised by Perkin and Trikojus (*J.*, 1926, 2925) and by Groenewoud and Robinson (*J.*, 1936, 199).

Dijksman and Newbold (Part I, *J.*, 1951, 1213) prepared rhodanine condensation products from the methyl esters of phthalaldehydic and opianic acid and then proceeded by alkaline treatment of these intermediates to the 1 : 2-dihydro-1-keto-2-thianaphthalene-3-carboxylic acids. In order to obviate the preparation of such methyl esters, the direct condensation of opianic acid with rhodanine in acetic acid in the presence of sodium acetate was examined; under these conditions 2-carboxyacetophenone gave 5-(*o*-carboxy-α-methylbenzylidene)rhodanine (*loc. cit.*). Surprisingly, opianic acid gave a monosodium salt of 5-(2-carboxy-3 : 4-dimethoxybenzylidene)rhodanine, from which the free acid could be liberated by dissolution of the salt in aqueous sodium carbonate followed by acidification with mineral acid. Both the sodium salt and the free rhodanine acid were converted into 1 : 2-dihydro-1-keto-7 : 8-dimethoxy-2-thianaphthalene-3-carboxylic acid by hot aqueous sodium hydroxide. Reaction of *m*-opianic acid and 4 : 5-methylene-

dioxyphthalaldehydic acid with rhodanine gave the sodium salts of the respective rhodanine derivatives (I; R = CO_2H, R' = CH:C·CO·NH·CS·S) and (IV; R = CO_2H, R' = CH:C·CO·NH·CS·S), from which the free rhodanine acids were liberated for characterisation The respective sodium salts were directly converted into 1 : 2-dihydro-1-keto-6 : 7-dimethoxy- (II) and -6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid (V) by heating them with alkali; (II) and (V) were characterised as their methyl esters.

Reduction of (II) and (V) in boiling ethanol with Raney nickel gave respectively 5 : 6-dimethoxy- (III) and 5 : 6-methylenedioxy-indan-1-one (VI). The crude products in both cases gave a blue colour with concentrated sulphuric acid in acetic acid, a very sensitive and specific test for *o*-vinyl-aldehydes (Bick, Ewen, and Todd, *J.*, 1949, 2767; Bick and Todd, *J.*, 1950, 1606), though the intensity of the colour compared with that given by hydrastal (IV; R = CH:CH_2, R' = CHO) indicated the presence of only traces of such compounds; no 4 : 5-dimethoxy-2-vinylbenzaldehyde (I; R = CH:CH_2, R' = CHO) or hydrastal could be isolated in the two experiments. A mechanism was suggested in Part II of this series (*loc. cit.*) for the conversion of the thianaphthalenecarboxylic acids into indanones based on that suggested by Wiley and Hobson (*J. Amer. Chem. Soc.*, 1949, **71**, 2429) for the cyclisation of *o*-formylcinnamic acid to indan-1-one. In the 4 : 5-methylenedioxyphthalaldehydic acid series this would be as below:



Hydrastal could be formed from the ion (IX) by addition of a proton. There is no possibility of indanone formation during the preparation of hydrastininium iodide (X) (Freund, *loc. cit.*) since, according to current views on the Hofmann elimination reaction (see Ingold and Hughes, *Trans. Faraday Soc.*, 1941, **37**, 657), loss of a proton from the 'onium hydroxide from (X) would give an intermediate (XI) which would lose trimethylamine to give hydrastal (IV; R = CH:CH_2, R' = CHO). We have found that hydrastal is isomerised to 5 : 6-methylenedioxyindan-1-one (VI) by boiling it in ethanol in the presence of Raney nickel; the reagent may effect the change from (IV; R = CH:CH_2, R' = CHO) to the ion (IX) by loss of a proton; the formation of (VI) could then occur by the scheme above. This direct conversion of (IV; R = CH:CH_2, R' = CHO) into (VI) suggests that the formation of indan-1-one by the action of Raney nickel on 1 : 2-dihydro-1-keto-2-thianaphthalene described in Part II (*loc. cit.*) may proceed by a similar mechanism, and that *o*-vinylbenzaldehyde could be an intermediate.

Catalytic reduction of hydrastal over palladium gives 6-ethylpiperonaldehyde (IV; R = Et, R' = CHO), isolated as its 2 : 4-dinitrophenylhydrazone (cf. Späth, Schmid, and Sternberg, *Ber.*, 1934, **67**, 2095, who reduced the vinyl group in the analogous norcotarnone).

Experimental

m-*Meconin*.—This compound was prepared from veratric acid according to Perkin (*J.*, 1925, **127**, 195) in 12% yield. A specimen crystallised from aqueous ethanol as needles, m. p. 158°, having light absorption in ethanol: Max. at 220 (ε = 24,100), 258 (ε = 9400), and 294 mμ (ε = 7200).

5 : 6-*Methylenedioxyphthalide*.—By the method given in *Org. Synth.*, Coll. Vol. II, p. 55, for

the azlactone of veratraldehyde, piperonal gave 5-(3 : 4-methylenedioxybenzylidene)-2-phenyloxazol-4-one, m. p. 196—197° (Kropp and Decker, *Ber.*, 1909, **42**, 1188, give m. p. 197°), in 90% yield; the latter was converted into ethyl homopiperonylate, b. p. 130°/2 mm. (Keimatsu, *J. Pharm. Soc. Japan*, 1933, **53**, 1070, gives b. p. 145—147°/8 mm.), in 50% yield by the method described for ethyl homoveratrate (*Org. Synth.*, Coll. Vol. II, p. 333). Hydrolysis gave homopiperonylic acid, m. p. 127° (95%) (Mauthner, *Annalen*, 1909, **370**, 368, gives m. p. 127°), which by the method of Stevens (*loc. cit.*) and Stevens and Robertson (*loc. cit.*) gave 5 : 6-methylenedioxyphthalide as needles, m. p. 188—189° (lit., m. p. 188—189°) from aqueous ethanol. It showed light absorption in ethanol : Max. at 220 (ε = 21,800), 256 (ε = 5400), and 298 mμ (ε = 7300).

4 : 5-*Methylenedioxyphthalide.*—Piperonylic acid (45 g.) was heated with hydrochloric acid (200 c.c.; *d* 1·19) and formaldehyde (45 c.c.; 40%) on the steam-bath for 12 hours. The reaction mixture was diluted with an equal volume of water and filtered from unchanged piperonylic acid (40 g.). The filtrate gradually deposited a solid (1·0 g.), m. p. *ca.* 135°, which after five crystallisations from aqueous ethanol gave 4 : 5-*methylenedioxyphthalide* (100 mg.) as long fine needles, m. p. 176—178°, depressed to 145—150° on mixture with 5 : 6-methylenedioxyphthalide [Found: C, 60·7; H, 3·5%; *M* (Rast), 192. $C_9H_6O_4$ requires C, 60·7; H, 3·4%; *M*, 178]. Light absorption in ethanol: Max. at 224 (ε = 25,100), 270 (ε = 6250), and 294 mμ (ε = 4900). The compound is more soluble in water than the 5 : 6-isomer, but dissolves in 5% aqueous potassium hydroxide on warming and is precipitated from the cold solution on acidification with hydrochloric acid. It dissolves in aqueous sodium carbonate on warming, crystallising out on cooling.

m-*Opianic Acid.*—A solution of *m*-meconin (10 g.) in dry benzene (250 c.c.) was distilled until 50 c.c. of distillate were collected and then treated successively with dry carbon tetrachloride (200 c.c.) and *N*-bromosuccinimide (18·5 g.). The mixture was heated under reflux on the steam-bath for 2 hours while irradiated with a 60-watt lamp adjacent to the flask. The cooled reaction mixture was filtered from succinimide, and the filtrate evaporated under reduced pressure to give a yellow oil, which was stirred with water (250 c.c.) on the steam-bath for 1 hour. The yellow solution was decanted from tar, heated on the steam-bath, and treated with aniline, added in portions until an excess was present. Methanol (50 c.c.) was added, and the mixture allowed to cool. The aniline compound was separated, washed with methanol (20 c.c.), and dried (13·5 g.; m. p. 213—214°; Fargher and Perkin, *loc. cit.*, give m. p. 213—214°). The aniline compound was hydrolysed by heating it with hydrochloric acid (100 c.c.; 3N) on the steam-bath for 30 min. The crude *m*-opianic acid which separated on cooling was purified by digestion with saturated aqueous sodium carbonate, filtration, and acidification of the filtrate (Congo-red) with 3N-hydrochloric acid, giving *m*-opianic acid (6·9 g., 65%; m. p. 183°). A specimen, once crystallised from water (charcoal), separated as needles, m. p. 187—188° (Fargher and Perkin, and Chakravarti and Swaminathan, *locc. cit.*, give m. p. 187—188°) (Found : C, 57·4; H, 5·0%; equiv., 208. Calc. for $C_{10}H_{10}O_5$: C, 57·15; H, 4·8%; equiv., 210). Light absorption in ethanol : Max. at 224 (ε = 18,400), 243 (ε = 11,100), and 292 mμ (ε = 7200).

4 : 5-*Methylenedioxyphthalaldehydic Acid.*—5 : 6-Methylenedioxyphthalide was treated with *N*-bromosuccinimide, and the product hydrolysed. The crude acid was isolated as the aniline compound (m. p. 185—186°; Chakravarti, Swaminathan, and Venkataraman, *loc. cit.*, give m. p. 187°) which after treatment as described above gave 4 : 5-methylenedioxyphthalaldehydic acid, m. p. 164—166° (72% yield). A sample crystallised from water in needles, m. p. 167° (*idem*, *ibid.*, give m. p. 167°) (Found : C, 55·9; H, 3·2%; equiv., 198. Calc. for $C_9H_6O_5$: C, 55·7; H, 3·1%; equiv., 194). Light absorption in ethanol : Max. at 224 (ε = 18,800), 240 (ε = 4300), 260 (ε = 4600), and 300 mμ (ε = 6400).

Condensation of Opianic Acid and Rhodanine (with D. J. Dijksman).—Opianic acid (10·0 g.), rhodanine (6·0 g.), fused sodium acetate (12·0 g.), and glacial acetic acid (30 c.c.) were heated together under reflux for 30 minutes, and the hot reaction mixture was poured into cold water (500 c.c.). The yellow solid (16·0 g.) which separated was insoluble in the common organic solvents but crystallised from water, to give the *tetrahydrate* of a monosodium salt of 5-(2-carboxy-3 : 4-dimethoxybenzylidene)rhodanine as yellow needles, decomposing at *ca.* 220° (Found : C, 39·55; H, 4·5%; equiv., 420. $C_{13}H_{10}O_5NS_2Na,4H_2O$ requires C, 39·45; H, 4·5%; equiv., 419). A solution of the sodium salt in cold 10% aqueous sodium carbonate was poured into excess of dilute hydrochloric acid, and the precipitate crystallised from aqueous ethanol, to give 5-(2-*carboxy*-3 : 4-*dimethoxybenzylidene*)*rhodanine* as small, light yellow prisms, m. p. 237—240° (decomp.) (Found : C, 47·8; H, 3·5%; equiv., 167. $C_{13}H_{11}O_5NS_2$ requires C, 48·0; H, 3·4%; equiv., 162·5). Light absorption in water : Max. at 270 (ε = 9400) and 286 mμ

(ε = 9800); in 0·1N-sodium hydroxide: Max. at 374 (ε = 17,800) and inflection at 258 mμ (ε = 8100); cf. light absorption of 1 : 2-dihydro-1-keto-7 : 8-dimethoxy-2-thianaphthalene-3-carboxylic acid in 0·1N-sodium hydroxide: Max. at 329 mμ (ε = 15,000).

1 : 2-*Dihydro*-1-*keto*-7 : 8-*dimethoxy*-2-*thianaphthalene*-3-*carboxylic Acid.*—(*a*) The sodium salt above (1·0 g.) was heated on the steam-bath for 30 minutes with 15% sodium hydroxide solution (10 c.c.), and the cooled reaction mixture poured into excess of 3N-hydrochloric acid. Crystallisation of the precipitate from ethanol gave the thianaphthalene acid (0·5 g.) as small needles, m. p. 257—258°, undepressed by a specimen prepared as described in Part I (*loc. cit.*) (Found: C, 54·3; H, 3·7. Calc. for $C_{12}H_{10}O_5S$: C, 54·1; H, 3·8%). (*b*) 5-(2-Carboxy-3 : 4-dimethoxybenzylidene)rhodanine under the same conditions as in (*a*) gave the thianaphthalene acid (50%) as small needles (from ethanol), m. p. 256—257°, undepressed by preparation (*a*) (Found: C, 54·0; H, 3·5%).

5-(2-*Carboxy*-4 : 5-*dimethoxybenzylidene*)*rhodanine.*—*m*-Opianic acid (4·0 g.), rhodanine (2·6 g.), and fused sodium acetate (8·0 g.) in glacial acetate acid (50 c.c.) were heated under reflux for 30 minutes. The solution was poured into water (300 c.c.); the precipitated sodium salt (4·3 g.) was separated, and a portion dissolved in 20% aqueous sodium carbonate in the cold, filtered, and acidified (Congo-red) with 3N-hydrochloric acid. Crystallisation of the precipitate from ethanol gave 5-(2-*carboxy*-4 : 5-*dimethoxybenzylidene*)*rhodanine* as yellow needles, m. p. 260° (decomp.) (Found: C, 48·0; H, 3·1. $C_{13}H_{11}O_5NS_2$ requires C, 48·0; H, 3·4%). Light absorption in ethanol: Max. at 215 (ε = 18,500), 252 (ε = 14,200), 268 (ε = 12,900), 290 (ε = 11,500), and 386 mμ (ε = 22,000).

5-(2-*Carboxy*-4 : 5-*methylenedioxybenzylidene*)*rhodanine.*—By the above method 4 : 5-methylenedioxyphthalaldehydic acid (4·0 g.) gave the sodium salt (4·8 g., 70%). The free acid, 5-(2-*carboxy*-4 : 5-*methylenedioxybenzylidene*)*rhodanine*, separated from aqueous ethanol as needles, m. p. 256—257° (decomp.) (Found: C, 46·6; H, 2·3. $C_{13}H_7O_5NS_2$ requires C, 46·6; H, 2·3%). Light absorption in ethanol: Max. at 208 (ε = 18,300), 222 (ε = 18,500), 253 (ε = 13,400), 294 (ε = 14,500), and 385 mμ (ε = 13,400).

1 : 2-*Dihydro*-1-*keto*-6 : 7-*dimethoxy*-2-*thianaphthalene*-3-*carboxylic Acid.*—The sodium salt of 5-(2-carboxy-4 : 5-dimethoxybenzylidene)rhodanine (4·1 g.) was heated under reflux for 1 hour with 15% aqueous sodium hydroxide (60 c.c.). The cooled solution was poured into excess of dilute hydrochloric acid, and the precipitate separated. Crystallisation from ethanol gave 1 : 2-*dihydro*-1-*keto*-6 : 7-*dimethoxy*-2-*thianaphthalene*-3-*carboxylic acid* (3·35 g.) as fine yellow needles, m. p. 306—307° (Found: C, 53·8; H, 3·9; S, 11·8%; equiv., 262. $C_{12}H_{10}O_5S$ requires C, 54·1; H, 3·8; S, 12·0%; equiv., 266). Light absorption in ethanol: Max. at 232 (ε = 13,700), 272 (ε = 36,500), 328 (ε = 7600), 350 (ε = 8750), and 366 mμ (ε = 7600). Esterification by ethereal diazomethane gave the *methyl* ester, which formed light yellow, felted needles, m. p. 212°, from methanol (Found: C, 55·9; H, 4·5; S, 9·8. $C_{13}H_{12}O_5S$ requires C, 55·7; H, 4·3; S, 10·2%). Light absorption in ethanol: Max. at 232 (ε = 10,400), 258 (ε = 26,400), 276 (ε = 34,100), 284 (ε = 30,100), 338 (ε = 8950), 352 (ε = 10,600), and 368 mμ (ε = 9650).

1 : 2-*Dihydro*-1-*keto*-6 : 7-*methylenedioxy*-2-*thianaphthalene*-3-*carboxylic acid*, prepared as above from the sodium salt of the corresponding rhodanine in 70% yield, formed needles, m. p. 335—336° (decomp.), from ethanol (Found: C, 52·7; H, 2·7. $C_{11}H_6O_5S$ requires C, 52·8; H, 2·4%). Light absorption in ethanol: Max. at 252 (ε = 27,000), 262 (ε = 21,300), 270 (ε = 22,800), 274 (ε = 23,500), 332 (ε = 5900), 350 (ε = 6400), and 364 mμ (ε = 5200). The *methyl* ester separated from ethanol as light yellow needles, m. p. 228—229° (Found: C, 54·5; H, 3·2; S, 11·9. $C_{12}H_8O_5S$ requires C, 54·5; H, 3·0; S, 12·1%). Light absorption in ethanol: Max. at 208 (ε = 8000), 255 (ε = 32,200), 271 (ε = 25,400), 276 (ε = 28,200), 288 (ε = 23,100), 352 (ε = 9100), and 370 mμ (ε = 7800).

5 : 6-*Dimethoxyindan*-1-*one.*—1 : 2-Dihydro-1-keto-6 : 7-dimethoxy-2-thianaphthalene-3-carboxylic acid (3·0 g.) was heated under reflux for 6 hours with a suspension of Raney nickel (34 g.; W.6, prepared according to *Org. Synth.*, **29**, 25) in ethanol (100 c.c.). After removal of the nickel and nickel sulphide, the filtrate and ethanol washings were evaporated to small bulk under reduced pressure, diluted with water (200 c.c.), and extracted with ether (4 × 50 c.c.). The combined ethereal extract was washed with 2N-sodium hydroxide and water and dried (Na_2SO_4). Removal of the ether gave a solid (300 mg.) which gave a blue colour in glacial acetic acid solution with concentrated sulphuric acid. Crystallisation of the solid from benzene–light petroleum (b. p. 40—60°) gave 5 : 6-dimethoxyindan-1-one as needles, m. p. 116—117°, undepressed when mixed with a specimen prepared as described by Perkin and Robinson (*J.*, 1907, **91**, 1080) (Found: C, 68·6; H, 6·3. Calc. for $C_{11}H_{12}O_3$: C, 68·7; H, 6·3%). Light absorption in ethanol: Max. at 230 (ε = 18,000), 268 (ε = 11,700), and 312 mμ (ε = 10,400).

5 : 6-*Methylenedioxyindan-1-one*.—1 : 2-Dihydro-1-keto-6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid (3·5 g.) and Raney nickel (35 g.) in ethanol (70 c.c.) were heated under reflux for 8 hours. The reaction mixture was worked up as in the previous experiment. The solid residue (1·0 g.) after removal of ether gave a blue colour in the sulphuric–acetic acid test. Crystallisation from benzene–light petroleum (b. p. 40—60°) gave prismatic needles, m. p. 156—158° (300 mg.), which on further crystallisation from the same solvent and sublimation at 120°/10^{-4} mm. gave 5 : 6-methylenedioxyindan-1-one, m. p. 164—165° (Found : C, 67·8; H, 4·8. Calc. for $C_{10}H_8O_3$: C, 68·1; H, 4·5%). Light absorption in ethanol : Max. at 208 (ε = 16,000), 229 (ε = 16,500), 265 (ε = 7500), and 315 mμ (ε = 10,000). It was undepressed on mixing with a specimen prepared from β-(4 : 5-methylenedioxyphenyl)propionic acid according to Perkin and Robinson (*loc. cit.*), which separated from benzene as prismatic needles, m. p. 164—165° (lit., m. p. 160°) (Found : C, 68·25; H, 4·7%). The compound gave a crimson colour with concentrated sulphuric acid. The 2 : 4-*dinitrophenylhydrazone* separated from benzene as bright red needles, m. p. 265—266° (decomp.) (Found : C, 54·3; H, 3·4; N, 15·7. $C_{16}H_{12}O_6N_4$ requires C, 53·9; H, 3·4; N, 15·7%). Light absorption in chloroform : Max. at 246 (ε = 18,300), 316 (ε = 7950), 334 (ε = 7950), and 404 mμ (ε = 32,700).

Preparation of Hydrastal from Cotarnine.—Hydrocotarnine. Freund and Dormeyer's procedure (*Ber.*, 1891, **24**, 2734) lacks detail; the following method proved satisfactory. A solution of cotarnine chloride (50 g.) in water (250 c.c.) was stirred vigorously for 6 hours with sodium amalgam (450 g.; 8%), the solution being kept acid (Congo-red) by frequent additions of 5N-sulphuric acid. The solution was made alkaline with 3N-sodium hydroxide and extracted with ether (3 × 150 c.c.), the combined extracts being washed with water (100 c.c.) and dried (Na_2SO_4). Removal of the ether gave hydrocotarnine (20·0 g.) as an oil which solidified when kept at 0° overnight. The product had m. p. 55—56° (lit., m. p. 55·5—56·5°) and gave a yellow colour with concentrated sulphuric acid in the cold, becoming deep purple on warming.

Hydrastinine hydriodide. In our hands the oxidation of hydrohydrastinine [prepared from hydrocotarnine according to Pyman and Remfry (*J.*, 1912, **101**, 1595) in 30% yield] by potassium dichromate and dilute sulphuric acid, as recommended by Freund and Will (*Ber.*, 1887, **20**, 2403), proved very unsatisfactory. The following method, a modification of that of Topchiev (*J. Applied Chem. U.S.S.R.*, 1933, **6**, 529), was used. Hydrohydrastinine (13·5 g.) and freshly fused sodium acetate (9·5 g.) were heated under reflux in ethanol (34 c.c.) and treated with a solution of iodine (21·6 g.) in ethanol (210 c.c.), added dropwise during 1 hour. The solution was kept overnight at room temperature, and the solid (22 g.) which separated was filtered off and added in small amounts to a solution of sodium dithionite (hydrosulphite) (7·0 g.) in water (50 c.c.). The solution was warmed and filtered, hydrastinine hydriodide (15 g.) separating as yellow needles, m. p. 231—233° (lit., m. p. 233—234°), on cooling.

Hydrastinine methiodide. Hydrastinine (8·0 g.) was heated under reflux with methyl iodide (40 c.c.) for 1 hour. The excess of methyl iodide was removed under reduced pressure, and the residue crystallised twice from water to give hydrastinine methiodide (5·0 g.) as yellow needles, m. p. 262—264° (Freund, *loc. cit.*, gives m. p. 267°).

Hydrastal. Hydrastinine methiodide (5·0 g.) was heated on the steam-bath with 10% aqueous potassium hydroxide (90 c.c.) for 15 minutes; trimethylamine was evolved and an oil (2·7 g.) separated which solidified on cooling. Crystallisation from light petroleum (b. p. 60—80°) gave hydrastal (2·0 g.) as plates, m. p. 76—78° (Freund, *loc. cit.*, gives 78—79°). The compound gave an intense deep blue colour in acetic acid with concentrated sulphuric acid. It showed light absorption in ethanol : Max. at 206 (ε = 8600), 248 (ε = 27,700), 300 (ε = 6700), and 328 mμ (ε = 6700). The 2 : 4-*dinitrophenylhydrazone* separated from benzene as small red prisms, m. p. 227—228° (decomp.) (Found : C, 54·1; H, 3·6; N, 15·9. $C_{16}H_{12}O_6N_4$ requires C, 53·9; H, 3·3; N, 15·7%). Light absorption in chloroform: Max. at 250 (ε = 22,500), 314 (ε = 9000), and 396 mμ (ε = 47,900).

5 : 6-*Methylenedioxyindan-1-one from Hydrastal*.—A solution of hydrastal (500 mg.) in ethanol (10 c.c.) was heated under reflux with Raney nickel (4 g.) for 4 hours. The filtrate and washings from the catalyst were concentrated under reduced pressure to 5 c.c. and diluted with water (50 c.c.), and the mixture was extracted with ether (3 × 25 c.c.). The dried (Na_2SO_4) ethereal extract was evaporated, to give a colourless oil (450 mg.) which gave no colour with the sulphuric–acetic acid test, but gave a crimson colour with concentrated sulphuric acid. Since the product showed no signs of solidification, it was dissolved in methanol (10 c.c.) and treated with Brady's reagent, and the resulting precipitate (500 mg.) crystallised three times from benzene, to give 5 : 6-methylenedioxyindan-1-one 2 : 4-dinitrophenylhydrazone as fine red needles, m. p. 266—

267° (decomp.) alone or mixed with a specimen of the authentic derivative (Found: C, 54·3; H, 3·5. Calc. for $C_{16}H_{12}O_6N_4$: C, 53·9; H, 3·4%). Light absorption in chloroform: max. at 246 (ε = 17,000), 316 (ε = 7800), 332 (ε = 7800), and 404 mμ (ε = 29,400).

6-Ethylpiperonaldehyde 2 : 4-Dinitrophenylhydrazone.—A solution of hydrastal (500 mg.) in methanol (80 c.c.) was shaken for 15 minutes with previously reduced 3% palladium–calcium carbonate catalyst at room temperature and pressure with hydrogen, after which time 68 c.c. had been absorbed (Calc. for 1 mol.: 68 c.c.). The filtered solution was evaporated under reduced pressure to give a clear viscous oil, which gave a dark red colour rapidly assuming a green-brown hue with concentrated sulphuric acid on warming. With sulphuric–acetic acid similar behaviour was shown. A portion of the oil on treatment in methanol with Brady's reagent gave *6-ethylpiperonaldehyde 2 : 4-dinitrophenylhydrazone*, which separated from benzene as red needles, m. p. 236—237° (decomp.) (Found: C, 54·0; H, 4·3. $C_{16}H_{14}O_6N_4$ requires C, 53·6; H, 4·7%). Light absorption in chloroform: Max. at 246 (ε = 17,700), 312 (ε = 7450), and 388 mμ (ε = 28,700).

The authors thank Professor F. S. Spring, F.R.S., for his continued interest, the Governors of The Royal Technical College for the award of the Nobel Scholarship (to J. J. B.), and Messrs. T. and H. Smith, Ltd., for gifts of chemicals.

THE ROYAL TECHNICAL COLLEGE, GLASGOW. [*Received, June 23rd*, 1952.]

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844. *Friedel–Crafts Succinoylation of Anthracene. Synthesis of 1′- and 4′-Hydroxy-1 : 2-benzanthracene.*

By (MISS) R. SCHOENTAL.

Condensation of anthracene with succinic anhydride in the presence of aluminium chloride in cold methylene chloride yielded a mixture from which β-1-anthroylpropionic acid, m. p. 184—185°, and β-9-anthroylpropionic acid, m. p. 177°, have been isolated. The structure of the former acid has been proved by its conversion into the known 4′-hydroxy-1 : 2-benzanthracene; the latter acid was oxidised to anthraquinone and reduced to the known β-(9 : 10-dihydro-9-anthroyl)propionic acid. The product, m. p. 125°, believed to be β-1-anthroylpropionic acid (Bergmann and Weizmann, *J.*, 1938, 1243), was obviously a mixture.

β-2-Anthroylpropionic acid, which is a minor constituent of the mixture of products under the above conditions, has been converted into 1′-hydroxy-1 : 2-benzanthracene, the methyl ether of which was required for biological testing.

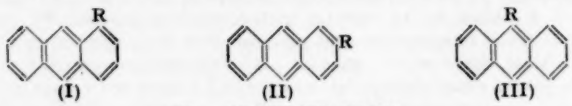
A disuccinoylation product of anthracene has also been isolated in small yield.

ANTHRACENE has been subjected to Friedel–Crafts condensations with succinic anhydride in nitrobenzene by several groups of workers (for references, see Berliner, *Org. Reactions*, 1949, **5**, 234) * but the course of the reaction has not been completely elucidated. Of the three theoretically possible monosubstitution products (I), (II), (III), only (II) has been consistently obtained. Berliner (*loc. cit.*), using benzene as solvent, recorded, without details, the isolation of β-(9 : 10-dihydro-9-anthroyl)propionic acid and Bergmann and Weizmann (*loc. cit.*) reported the isolation besides (II) of a second keto-acid, m. p. 125°, which they believed to be (I) but this structure is now shown to be incorrect.

From the published results it is evident that, equimolecular proportions of reactants being used, most of anthracene is recovered unchanged, and only about 20% could be accounted for in the form of (II). It seems therefore probable that condensation of anthracene with more than one molecule of succinic anhydride takes place. The isolation

* The product of condensation of anthracene with maleic anhydride in the presence of aluminium chloride (Oddy, *J. Amer. Chem. Soc.*, 1923, **45**, 2156) is recorded in this Review (p. 286) as a 9-substitution product, but it is obviously the well-known maleic anhydride adduct (Diels and Alder, *Annalen*, 1931, **486**, 191), as shown by its m. p. and that of the methyl ester.

of all the acidic components of a reaction product which may contain, besides the three isomeric monopropionic acids, some at least of the 15 possible di-isomers presents obvious difficulties: hence, the intractable mixtures which have often been encountered.



(I) (II) (III)

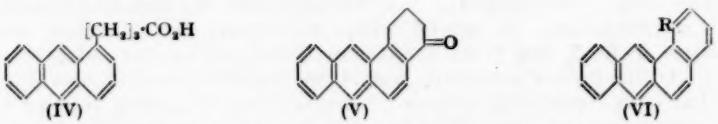
[R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$.]

Since methylene chloride proved advantageous as solvent in some Friedel–Crafts reactions, favouring α-substitution (Baddeley, *J.*, 1949, S 99), its use for this case has been studied. Although none of the reactants is readily soluble in methylene chloride, a homogeneous solution is rapidly formed even when a small volume of the cold solvent is used. The product is thereafter slowly deposited. As a low-boiling solvent, methylene chloride presents another obvious advantage over nitrobenzene, the removal of which by prolonged steam-distillation may have deleterious effects on sensitive keto-acids.

When 1—2 mols. of aluminium chloride were used, about half the anthracene remained unchanged; but use of 2 mols. each of succinic anhydride and aluminium chloride resulted in an almost complete transformation of anthracene into acidic products. However, the isolation of individual acids in this case was more difficult than from a product obtained under equimolecular conditions, and only the latter is here described.

Leaching of the mixture of acids with ethyl acetate left a small insoluble residue of disuccinoylation product, m. p. *ca.* 235° (decomp.), characterised by its methyl ester; the positions of substitution were not established. It formed an easily soluble sodium salt, whereas the acid (II), which is similar in appearance and m. p., forms a rather insoluble sodium salt. Acids (I) and (III) also form well-crystallised sodium salts, but only in the presence of excess of sodium ions. The monopropionic acids were separated by chromatography on silica from the other acidic products, which were strongly adsorbed. Acid (II) is less easily eluted than (I) and (III). Acid (I), the main product of the reaction, was readily obtained pure by crystallisation from ethyl acetate; acid (III), more soluble, remained in the mother-liquor, from which it was recovered on further concentration and was purified through its sodium salt and repeated crystallisation from benzene. Its structure was proved by oxidation to anthraquinone and by reduction to β-(9 : 10-dihydro-9-anthroyl)propionic acid.

Acid (I) was reduced to the corresponding butyric acid (IV), and the latter cyclised by the stannic chloride method (Fieser and Novello, *J. Amer. Chem. Soc.*, 1940, **62**, 1855) to 1′ : 2′ : 3′ : 4′-tetrahydro-4′-keto-1 : 2-benzanthracene (V), which yielded on dehydrogenation the known 4′-hydroxy-1 : 2-benzanthracene (Sempronj, *Gazzetta*, 1939, **69**, 448). This proves the structure of acid (I).



(IV) (V) (VI)

Similar dehydrogenation of 1′ : 2′ : 3′ : 4′-tetrahydro-1′-keto-1 : 2-benzanthracene (Cook and Robinson, *J.*, 1938, 505) yielded 1′-hydroxy-1 : 2-benzanthracene (VI; R = OH), the methyl ether of which was required for biological testing.

Experimental

Friedel–Crafts Succinoylation of Anthracene in Methylene Chloride and Separation of the Keto-acids.—Anthracene (71·4 g.) and succinic anhydride (40 g.) were ground finely together, suspended in methylene chloride (350 c.c.), and treated in an ice-bath with finely powdered, anhydrous aluminium chloride (55 g.) with constant shaking. The colourless suspension became dark red on the addition of aluminium chloride and after less than an hour the mixture formed a homogeneous dark red solution. It was then left at 0—4° overnight, and a sticky

precipitate was formed. Crushed ice, dilute hydrochloric acid, and ethyl acetate were then added, to decompose this complex. The orange-coloured suspension was freed from solvents on a water-bath, and the solid collected, washed free from aluminium salts, and leached with dilute potassium carbonate solution. The remaining unchanged anthracene was filtered off (about 30 g.). The acids obtained by acidification of the carbonate solution were collected, washed, dried, and leached with a small quantity of ethyl acetate. The insoluble residue (about 1·0 g.) was dissolved in dilute sodium carbonate solution and filtered, and the acid obtained on acidification of the filtrate was crystallised from " Cellosolve " (2-ethoxyethanol). This *acid*, a disuccinoylation product of anthracene, formed golden-yellow needles, m. p. *ca.* 235° (decomp.) (Found: C, 69·85; H, 5·1. $C_{22}H_{18}O_6$ requires C, 69·8; H, 4·8%). Its *dimethyl* ester, prepared in methanol by the action of ethereal diazomethane, crystallised from benzene in yellow, silky needles, m. p. 138—139·5° (Found: C, 71·0; H, 5·7. $C_{24}H_{22}O_6$ requires C, 70·9; H, 5·5%).

The ethyl acetate solution was freed from solvents *in vacuo*, and the residue dissolved in benzene and chromatographed on silica gel (200—300 mesh). The forerun, containing coloured, neutral, high-melting products, was discarded. The column on being washed with benzene developed a bright yellow zone (below a strongly adsorbed brown one) which was eluted with chloroform, and the extract concentrated *in vacuo*. The solid which slowly crystallised out was filtered off (see below); the mother-liquor was concentrated further, and the solid filtered off, dissolved in 10% sodium carbonate, treated with an approximately equal volume of saturated sodium chloride solution, and left in the cold; the sodium salt crystallised; it was collected and the recovered acid crystallised several times from benzene. β-9-*Anthroylpropionic acid* (III) formed small, yellowish prisms, m. p. (with some softening) 177° (Found: C, 78·0; H, 5·3. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%). Oxidation of this acid with chromic acid in glacial acetic acid yielded anthraquinone, and reduction for 16 hours by Martin's modification of Clemmensen's method (*J. Amer. Chem. Soc.*, 1936, **58**, 1438) gave the known β-(9 : 10-dihydro-9-anthroyl)propionic acid as colourless, lustrous scales (from benzene) or needles (from benzene–light petroleum), m. p. 163—163·5° (Found: C, 77·1; H, 5·9. Calc. for $C_{18}H_{16}O_3$: C, 77·1; H, 5·75%) (Cook, Robinson, and Roe, *J.*, 1939, 266, give m. p. 160—161°).

The solid obtained on concentration of the chloroform eluate from the yellow zone of the silica column was purified through its sodium salt and crystallised from ethyl acetate. β-1-*Anthroylpropionic acid* (I) formed golden-yellow, lustrous scales, m. p. 184—185° (Found: C, 77·5; H, 5·3. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%). Its *methyl* ester, obtained by use of ethereal diazomethane, formed yellow, transparent, heavy prisms, m. p. 65·5—66·5° (Found: C, 77·8; H, 5·6; OMe, 10·2. $C_{19}H_{16}O_3$ requires C, 78·0; H, 5·5; OMe, 10·6%). The acid recovered from the methyl ester had the same m. p., 184—185°.

Development of the dark zone of the silica column with chloroform yielded a small amount of the known β-2-anthroylpropionic acid (II), m. p. 223°.

γ-1-*Anthrylbutyric acid* (IV).—The keto-acid (I) (7·0 g.) was reduced by Martin's method (*loc. cit.*) for 28 hours. The reduced *acid* (IV) formed colourless needles (from benzene–light petroleum), m. p. 148—149° (Found: C, 81·8; H, 6·2. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

1′ : 2′ : 3′ : 4′-*Tetrahydro*-4′-*keto*-1 : 2-*benzanthracene* (V).—The foregoing acid (1·3 g.) in thiophen-free benzene (dried over sodium) (5 c.c.) was treated in an ice-bath with phosphorus pentachloride (1·2 g.) in benzene (5 c.c.), left for 2·5 hours at 0°, then treated with stannic chloride (2 c.c.) in benzene (2 c.c.). A deep violet precipitate separated immediately. After about 30 minutes in the ice-bath and a further 10 minutes at room temperature the complex was decomposed with ice and dilute hydrochloric acid. The product was extracted into benzene and purified by chromatography on alumina. 1′ : 2′ : 3′ : 4′-*Tetrahydro*-4′-*keto*-1 : 2-*benzanthracene* crystallised from methanol in almost colourless prismatic needles (0·80 g.), m. p. 196—197° (Found: C, 88·1; H, 5·7. $C_{18}H_{14}O$ requires C, 87·8; H, 5·7%). It formed an orange *picrate*, m. p. 163° (Found: N, 8·0. $C_{18}H_{14}O,C_6H_3O_7N_3$ requires N, 8·8%).

4′-*Hydroxy*-1 : 2-*benzanthracene*.—A solution of the foregoing ketone (160 mg.) in 1-methylnaphthalene (5 c.c.) was boiled under reflux in a nitrogen atmosphere with palladium black (30 mg.) for 16 hours. The product crystallised from benzene in colourless needles, m. p. 225° (decomp.), not depressed when mixed with a specimen prepared according to Sempronj (*loc. cit.*), and gave a methyl ether, m. p. 163°, not depressed by admixture with an authentic specimen.

1′-*Hydroxy*-1 : 2-*benzanthracene* (VI; R = OH).—1′ : 2′ : 3′ : 4′-Tetrahydro-1′-keto-1 : 2-benzanthracene, m. p. 114°, prepared from (II) according to Cook and Robinson (*J.*, 1938, 505), was dehydrogenated by boiling it (0·6 g.) in 1-methylnaphthalene (4 c.c.) in a nitrogen atmosphere with palladium black (60 mg.) for 18 hours. Crystallised from benzene–light petroleum, the *phenol* formed silky, yellowish needles, m. p. 168—170° (Found: C, 88·8; H, 4·5.

$C_{18}H_{12}O$ requires C, 88·5; H, 4·9%). Its *methyl ether*, prepared by the action of methyl sulphate and alkali and purified by chromatography on alumina from benzene–light petroleum, crystallised from methanol in colourless thin needles, m. p. 131—132° (Found: C, 88·0; H, 5·5; OMe, 11·5. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5; OMe, 12·0%), and gave a *s-trinitrobenzene* complex in the form of salmon-orange needles (from benzene), m. p. 188—189° (Found: N, 9·2. $C_{25}H_{17}O_7N_3$ requires N, 8·9%).

I am indebted to the British Empire Cancer Campaign for a grant which supported this work. I thank Dr. P. R. Peacock for interest in this work and Miss E. P. McLaren for valuable technical assistance. Microanalyses were by Drs. Weiler and Strauss, Oxford.

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GLASGOW, C.3. [*Received, August 14th*, 1952.]

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845. *Tetrahydroquinoxalines. A New Route from o-Amino-N-2′-hydroxyethylanilines.*

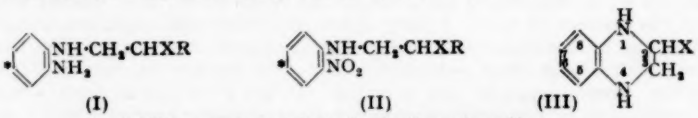
By G. R. RAMAGE and G. TRAPPE.

Cyclisation of some derivatives of *o*-amino-*N*-2′-hydroxyethylanilines (I) is described and provides a convenient route to 1 : 2 : 3 : 4-tetrahydroquinoxaline (III; X = H) and its 6-nitro-derivative.

IN connection with similar work on pyrimidine derivatives described in the following paper, an investigation was undertaken of the preparation of 1 : 2 : 3 : 4-tetrahydroquinoxalines by the cyclisation of *o*-amino-*N*-2′-hydroxy- and -chloro-ethylanilines (I; R = OH or Cl, X = H). This was necessitated by the striking difference in behaviour of 5-amino-2-chloro-4-2′-hydroxyethylaminopyrimidine and its 6-methyl derivative towards hydriodic acid, and also in order to investigate conditions which would allow cyclisation of the former.

The ready ring closure of 2-*o*-aminophenylethyl alcohol to dihydroindole under mild conditions has been reported by Bennett and Hafez (*J.*, 1941, 287), who later (*ibid.*, p. 652) indicated that the reaction proceeds through the intermediate *o*-aminophenylethyl chloride which was not, however, detected.

1 : 2 : 3 : 4-Tetrahydroquinoxaline was first prepared by reaction of catechol and ethylenediamine (Merz and Ris, *Ber.*, 1887, **20**, 1190) but the yield is variable and the product impure (Cavagnol and Wiselogle, *J. Amer. Chem. Soc.*, 1947, **69**, 795). Tetrahydro-2-methylquinoxaline was similarly prepared from propylenediamine and catechol (Ris, *Ber.*, 1888, **21**, 378). The only other tetrahydroquinoxalines reported are those obtained by reduction of such quinoxalines as can be prepared from *o*-phenylenediamines and glyoxal or 1 : 2-diketones (see, *e.g.*, Gibson, *J.*, 1927, 342).



(I) (II) (III)

* NO_2 in route to tetrahydro-6-nitroquinoxaline.

Condensation of *o*-chloronitrobenzene with 2-aminoethanol to yield (II; R = OH, X = H) has been described by Kremer (*J. Amer. Chem. Soc.*, 1939, **61**, 1321) who used sodium carbonate without solvent but much *o*-chloroaniline was also formed. Hippchen used pyridine as solvent (*Chem. Ber.*, 1947, **80**, 263) but we found *n*-butanol to be most effective. Reduction of the nitro-group in (II; R = OH, X = H) has been described by Kremer (*loc. cit.*), who used stannous chloride and hydrochloric acid, but we found sodium disulphide to be preferable. Cyclisation failed under mild conditions, *e.g.*, with benzenesulphonyl chloride as used by Bennett and Hafez (*loc. cit.*), with boron trifluoride, or on prolonged refluxing with hydrochloric acid, alone or in the presence of zinc chloride or toluene-*p*-sulphonic acid. 1 : 2 : 3 : 4-Tetrahydroquinoxaline (III; X = H) was

readily available in good yield by the action of either hydrochloric acid at 150—160° or constant-boiling hydrobromic acid under reflux. The use of hydriodic acid was unsatisfactory since it results in hydrolytic fission to give *o*-phenylenediamine. Cyclisation can also be achieved by the conversion of (I; R = OH, X = H), by phosphorus oxychloride, into *o*-amino-*N*-2′-chloroethylaniline (I; R = Cl, X = H) which, without purification, was refluxed in ethanol to form the hydrochloride of (III; X = H). A more satisfactory alternative procedure involved the conversion of *N*-2′-hydroxyethyl-*o*-nitroaniline (II; R = OH, X = H) into the corresponding chloro-compound (II; R = Cl, X = H) with phosphorus oxychloride, followed by reduction with stannous chloride and hydrochloric acid to (I; R = Cl, X = H) which was cyclised in refluxing ethanol. Dehydrogenation of tetrahydroquinoxaline in the vapour phase occurred readily in the presence of palladium on charcoal and gave quinoxaline.

The method appeared to be capable of modification so as to make available tetrahydroquinoxalines with substituents in the heterocyclic ring. When, however, it was applied to the preparation of 1 : 2 : 3 : 4-tetrahydro-2-methylquinoxaline (III; X = Me), the cyclisation stage was much more difficult, so the overall yield was poor. Kremer (*loc. cit.*) described the preparation of (II; R = OH, X = Me) and its reduction to (I; R = OH, X = Me), but we prepared them essentially as above except that *o*-chloronitrobenzene was condensed with 2-hydroxypropylamine in *n*-butanol in the presence of sodium carbonate. Attempts to cyclise (I; R = OH, X = Me) were unsatisfactory, mild treatment giving much unchanged material and more drastic conditions causing hydrolytic fission to *o*-phenylenediamine. The remarkable ease of fission of (I; R = OH, X = Me) may be illustrated by the fact that it occurred to an appreciable extent on 2 hours' refluxing with constant-boiling hydrobromic acid, whereas with (I; R = OH, X = H) 9 hours' refluxing caused no apparent fission. The use of hydrobromic acid has given 1 : 2 : 3 : 4-tetrahydro-2-methylquinoxaline in low yield. The alternative procedure of first preparing the chloro-derivative (II; R = Cl, X = Me) by the action of phosphorus oxychloride, followed by reduction to *o*-amino-*N*-2′-chloro-*n*-propylaniline (I; R = Cl, X = Me) and cyclisation, was no more successful.

1 : 2 : 3 : 4-Tetrahydro-6-nitroquinoxaline was readily prepared by cyclisation of 2-amino-*N*-2′-chloroethyl-4-nitroaniline (I; R = Cl, X = H) in refluxing ethanol. The method used for the preparation of (I; R = Cl, X = H) was substantially that of Hippchen (*loc. cit.*): 2-aminoethanol was condensed with 1-chloro-2 : 4-dinitrobenzene in ethanol to give (II; R = OH, X = H); this was reduced with sodium disulphide to 2-amino-*N*-2′-hydroxyethyl-4-nitroaniline which on treatment with thionyl chloride gave the necessary intermediate.

Although the method described provides an alternative route to 1 : 2 : 3 : 4-tetrahydroquinoxaline and the only route to the 6-nitro-derivative, it is not yet satisfactory for the preparation of 2-alkyl derivatives. The methyl group in the side chain inhibits cyclisation to tetrahydroquinoxalines, and this can be compared with the corresponding effect of the 4(6)-methyl group in the pyrimidine ring, described in the following paper.

Experimental

Analyses marked • are by Drs. Weiler and Strauss, Oxford.

N-2′-*Hydroxyethyl*-o-*nitroaniline* (II; R = OH, X = H).—A mixture of *o*-chloronitrobenzene (31·5 g., 0·2 mol.) and ethanolamine (25·0 g., 0·41 mol.) in *n*-butanol (70 c.c.) was refluxed for 12 hours. The butanol was removed on the water-bath under reduced pressure, and the residue diluted with water (150 c.c.) and extracted with ether. The ethereal extracts were washed twice with dilute hydrochloric acid, once with dilute sodium carbonate solution, then with water, and dried (Na_2SO_4). The ether was removed and the residue crystallised from benzene to give *N*-2′-hydroxyethyl-*o*-nitroaniline (21·2 g.; 58% based on *o*-chloronitrobenzene), in massive, bright red prisms, m. p. 74—75°.

o-*Amino*-N-2′-*hydroxyethylaniline* (I; R = OH, X = H).—A solution of sulphur (6·4 g., 0·2 g.-atom) and sodium sulphide (48 g., 0·2 mole) in water (150 c.c.) was refluxed for 2 hours with *N*-2′-hydroxyethyl-*o*-nitroaniline (18·2 g., 0·1 mole). On cooling, *o*-amino-*N*-2′-hydroxyethylaniline (11·9 g., 78%) crystallised in colourless plates, m. p. 105—106°. It was unchanged

after being refluxed with hydriodic acid (*d* 1·7) for a short period but after 6 hours the isolated product on sublimation gave *o*-phenylenediamine, m. p. 99·5—101°.

N-2′-*Chloroethyl*-o-*nitroaniline* (II; R = Cl, X = H).—*N*-2′-Hydroxyethyl-*o*-nitroaniline (15 g.) was added to phosphorus oxychloride (75 c.c.) during 15 minutes, and the mixture heated for 1 hour on the water-bath. Excess of oxychloride was removed under reduced pressure, and the residue warmed with water (100 c.c.) to decompose any remaining. After cooling, the product was extracted with benzene, and the extracts were washed with sodium carbonate and dried (Na_2SO_4). Removal of the benzene and distillation of the residue *in vacuo* gave a fraction (11·8 g.), b. p. 145—150°/0·5 mm., which readily solidified to an orange-coloured solid, m. p. 55—57°, and on crystallisation from alcohol gave *N*-2′-chloroethyl-*o*-nitroaniline as needles, m. p. 59°. Karrer and Naef (*Helv. Chim. Acta*, 1936, **19**, 1029) record m. p. 59°.

1 : 2 : 3 : 4-*Tetrahydroquinoxaline* (III; X = H).—(*a*) *o*-Amino-*N*-2′-hydroxyethylaniline (2 g.) and concentrated hydrochloric acid (10 c.c.) were heated at 150—160° in a sealed tube for 15 hours. The resulting solution was taken to dryness, and the residue dissolved in water (15 c.c.). When the clarified (charcoal) solution was made strongly alkaline with solid potassium carbonate, 1 : 2 : 3 : 4-tetrahydroquinoxaline separated; it crystallised from *cyclo*hexane in colourless plates (0·93 g.), m. p. 98°, not depressed on admixture with material made by the method of Merz and Ris (*loc. cit.*) (Found: N, 20·8. Calc. for $C_8H_{10}N_2$: N, 20·9%). Extraction of the aqueous mother-liquors with ether gave a further quantity (0·15 g.).

(*b*) A solution of *o*-amino-*N*-2′-hydroxyethylaniline (5 g.) in hydrobromic acid (25 c.c.; *d* 1·6) was refluxed for 9 hours. On cooling, a hydrobromide separated which was filtered off and dissolved in water (20 c.c.), and the aqueous solution was made alkaline and gave 1 : 2 : 3 : 4-tetrahydroquinoxaline (2·78 g.), m. p. 98°.

(*c*) *o*-Amino-*N*-2′-hydroxyethylaniline (2 g.) and phosphorus oxychloride (10 c.c.) were heated on the water-bath for 30 minutes. Excess of oxychloride was removed under reduced pressure, and the residue dissolved in water (20 c.c.), made alkaline with potassium carbonate, and extracted with ether. The ethereal extracts were washed with water and dried (Na_2SO_4), and the ether was removed, finally at room temperature under reduced pressure. The residue was refluxed in ethanol (100 c.c.) for 5 hours, the solvent removed, and an aqueous solution made alkaline as above, giving 1 : 2 : 3 : 4-tetrahydroquinoxaline (0·35 g.).

(*d*) *N*-2′-Chloroethyl-*o*-nitroaniline (10 g.) was heated on the water-bath (gently at first) with a solution of stannous chloride (50 g.) in concentrated hydrochloric acid (50 c.c.) for 5—10 minutes. With cooling in an ice-bath, the almost colourless solution was made strongly alkaline with sodium hydroxide solution (30%) and extracted with ether. The procedure under (*c*) then gave crude *o*-amino-*N*-2′-chloroethylaniline (8·15 g.) which was heated under reflux in alcohol. The resulting tetrahydroquinoxaline (5·35 g.) was distilled at 1 mm., and the solid distillate on crystallisation gave 1 : 2 : 3 : 4-tetrahydroquinoxaline (3·38 g.), m. p. 98°.

Quinoxaline.—1 : 2 : 3 : 4-Tetrahydroquinoxaline (1·0 g.) was sublimed, by heating at 100°/10^{-4} mm., through a 30-cm. column of palladium–charcoal (0·7 g.; 30%) on glass-wool (1·5 g.) kept at 150°. The solid product (0·9 g.) collecting on a cold finger during 6 hours was crystallised from light petroleum (b. p. <40°) and had m. p. 28° as recorded for quinoxaline [monohydrate, m. p. 37° (Platt, *Nature*, 1946, **157**, 439); oxalate (from alcohol), m. p. 179°].

N-2′-*Hydroxy*-n-*propyl*-o-*nitroaniline* (II; R = OH, X = Me).—A mixture of *o*-chloronitrobenzene (15·75 g., 0·1 mole), 2-hydroxypropylamine (7·5 g., 0·1 mole), anhydrous sodium carbonate (11·5 g., 0·11 mole), and *n*-butanol (35 c.c.) was refluxed with stirring for 12 hours. The butanol was removed on the water-bath under reduced pressure, and the residue diluted with water (100 c.c.) and steam-distilled. The product remained as an oil which readily solidified on cooling and was filtered off, washed with water, and dried in a desiccator. Crystallisation from carbon tetrachloride gave yellow needles (13·0 g., 66% based on 2-hydroxypropylamine), m. p. 67—68°.

o-*Amino*-N-2′-*hydroxy*-n-*propylaniline* (I; R = OH, X = Me).—A suspension of *N*-2′-hydroxy-*n*-propyl-*o*-nitroaniline (19·6 g., 0·1 mole) in a solution of sodium sulphide (48 g., 0·2 mole) and sulphur (6·4 g., 0·2 g.-atom) in water (140 c.c.) was refluxed for 4 hours. On cooling, the suspended oil solidified to almost colourless plates, which were filtered off, washed with a little water, and dried in a desiccator. Crystallisation from benzene gave *o*-amino-*N*-2′-hydroxy-*n*-propylaniline as colourless plates (14·2 g., 86%), m. p. 88—89°.

N-2′-*Chloro*-n-*propyl*-o-*nitroaniline* (II; R = Cl, X = Me).—*N*-2′-Hydroxy-*n*-propyl-*o*-nitroaniline (10 g.) was added during 15 minutes to phosphorus oxychloride (50 c.c.), and the mixture heated for 1 hour on the water-bath before the excess of oxychloride was removed under reduced pressure. The residue was warmed gently with water (50 c.c.), cooled, and

extracted with ether. The combined extracts were washed with aqueous sodium carbonate and dried (Na_2SO_4), the solvent was removed, and the residue (9·3 g.) distilled. The fraction, b. p. 137—140°/0·2 mm., solidified, on cooling, to a yellow solid (6·95 g.), m. p. 29—32°. *N*-2′-*Chloro*-n-*propyl*-o-*nitroaniline* was obtained as yellow-orange plates, m. p. 40°, by crystallisation from an equal volume of ether (*Found: C, 50·0; H, 4·8; Cl, 16·5. $C_9H_{11}O_2N_2Cl$ requires C, 50·4; H, 5·2; Cl, 16·5%).

1 : 2 : 3 : 4-*Tetrahydro*-2-*methylquinoxaline* (III; X = Me).—(*a*) A solution of *o*-amino-*N*-2′-hydroxy-*n*-propylaniline (1 g.) in hydrobromic acid (4 c.c.; *d* 1·6) was refluxed for 9 hours, then diluted with acetone (10 c.c.), and the hydrobromide (0·55 g.) filtered off, dissolved in water (3 c.c.), and made alkaline with saturated potassium carbonate solution. A white solid (0·2 g.) separated, which was filtered off and dried, and on crystallisation from *cyclo*hexane gave 1 : 2 : 3 : 4-tetrahydro-2-methylquinoxaline, m. p. 67—69°, raised to m. p. 71° on recrystallisation from light petroleum (b. p. 40—60°). Ris (*loc. cit.*) records m. p. 72°.

(*b*) *N*-2′-Chloro-*n*-propyl-*o*-nitroaniline (10 g.) was reduced with stannous chloride, the recovered oil heated under reflux in alcohol, and the product (6·51 g.) isolated by ether as previously described. After distillation through a 3″ Vigreux column the fraction (2·6 g.), b. p. 150—170°/5 mm., partly solidified on cooling. On sublimation at 130—140°/4 mm., a slightly sticky solid (1·15 g.) was obtained, which on crystallisation from light petroleum (b. p. 40—60°) gave 1 :2 : 3 : 4-tetrahydro-2-methylquinoxaline (0·43 g.) as white plates which darkened slowly in air and had m. p. 67—68°, raised to 71° on further recrystallisation.

N-2′-*Hydroxyethyl*-2 : 4-*dinitroaniline* (II; R = OH, X = H) (cf. Hippchen, *loc. cit.*).—A solution of 2-aminoethanol (12·5 g., 0·2 mole) in ethanol (20 c.c.) was added slowly (1 hour) with stirring to a solution of 1-chloro-2 : 4-dinitrobenzene (20·25 g., 0·1 mole) in ethanol (30 c.c.) at 60°; the solution was then kept at room temperature and finally refluxed for a further hour and, while hot, diluted with water (50 c.c.) to incipient turbidity. On cooling, *N*-2′-hydroxyethyl-2 : 4-dinitroaniline (20·8 g., 92%) separated as large yellow needles, which were filtered off, washed with a little aqueous alcohol (60%), and dried; m. p. 89—91°.

2-*Amino*-N-2′-*hydroxyethyl*-4-*nitroaniline* (I; R = OH, X = H).—A solution of sodium sulphide (25·2 g., 0·105 mole) and sulphur (3·4 g., 0·104 g.-atom) in water (65 c.c.) was added to *N*-2′-hydroxyethyl-2 : 4-dinitroaniline (22·7 g., 0·1 mole) in aqueous alcohol (80%; 150 c.c.) under reflux during 30 minutes, and refluxing continued for a further 5 hours. Alcohol (110 c.c.) was distilled off on the water-bath and, on cooling, 2-amino-*N*-2′-hydroxyethyl-4-nitroaniline separated as brown needles, which were filtered off, washed with aqueous alcohol (50%), and dried (15·2 g., 78%; m. p. 134—135°). Further crystallisation from water gave orange-brown needles, m. p. 135°.

2-*Amino*-N-2′-*chloroethyl*-4-*nitroaniline* (I; R = Cl, X = H) (cf. Hippchen, *loc. cit.*).—The foregoing amine (5 g.) was added to thionyl chloride (15 c.c.) at room temperature. After the initial vigorous evolution of gas had ceased, the mixture was heated on a water-bath for 5—10 minutes until all the solid had dissolved. Excess of thionyl chloride was removed on the water-bath under reduced pressure, and the residue treated with ice-water (100 c.c.) and made alkaline with aqueous ammonia. The product was extracted with ether, and the ethereal extracts were washed with water, dried, and evaporated to 25 c.c. After cooling, filtration gave 2-amino-*N*-2′-chloroethyl-4-nitroaniline (5·05 g., 92·5%), m. p. 113—115°, which on crystallisation from methanol gave bright prisms with a blue reflex, m. p. 115—116°.

1 : 2 : 3 : 4-*Tetrahydro*-6-*nitroquinoxaline* (III; X = H).—2-Amino-*N*-2′-chloroethyl-4-nitroaniline (10 g.) was refluxed in ethanol (500 c.c.) for 30 hours. Evaporation to *ca.* 60 c.c. gave the hydrochloride, which separated and was filtered off and dissolved in water (100 c.c.); the free base (6·8 g.) was precipitated with aqueous ammonia as an oil which solidified on cooling. Crystallisation from benzene gave 1 : 2 : 3 : 4-*tetrahydro*-6-*nitroquinoxaline* as broad red needles with a green reflex, m. p. 116° (*Found: C, 54·0; H, 5·1. $C_8H_9O_2N_3$ requires C, 53·6; H, 5·1%). The *picrate* crystallised from ethanol in ochre-coloured prisms, m. p. 180° (decomp.) (*Found: N, 20·6. $C_{14}H_{12}O_9N_6$ requires N, 20·6%).

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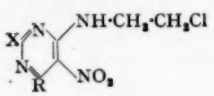
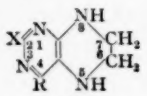
846. *Glyoxalinopyrimidines. The Cyclisation of Some 4-2′-Chloroethylaminopyrimidines.*

By G. R. RAMAGE and G. TRAPPE.

Preparations of 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine (I; R = H, X = Cl) and its 6-methyl derivative (I; R = Me, X = Cl) are described. The corresponding 5-amino-derivatives obtained on reduction have been shown to undergo cyclisation involving a pyrimidine-ring nitrogen atom in preference to the 5-amino-group. The resulting products are 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidines (VI; R = H or Me, X = Cl) and not derivatives of pteridine.

THIS paper describes an investigation into the reduction and cyclisation of 4-2′-chloroethylamino-5-nitropyrimidines (I), which was undertaken with a view to the synthesis of 5 : 6 : 7 : 8-tetrahydropteridines (II). Recently such a structure has been proposed for folinic acid, a factor isolated from liver, which stimulates the growth of *Leuconostoc citrovorum* and is closely related to pteroylglutamic acid (May *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 3067; Pohland *et al.*, *ibid.*, p. 3247). A similar approach to the synthesis of pteridine derivatives is the reduction and cyclisation of pyrimidine esters of type (III) (Boon, Jones, and Ramage, *J.*, 1951, 96) and related ketones (Boon and Jones, *ibid.*, p. 591), giving 7 : 8-dihydropteridines (IV).


(I)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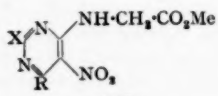
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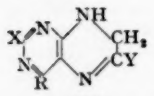
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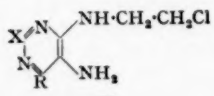
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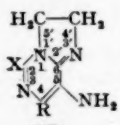

(VI)

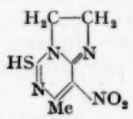
4-2′-Chloroethylamino-5-nitropyrimidines (I), however, after reduction to the corresponding 5-amino-compounds (V) could cyclise either (*a*) through the 5-amino-groups to give 5 : 6 : 7 : 8-tetrahydropteridines (II) or (*b*) by involving the pyrimidine nitrogen to give 5-amino-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine derivatives (VI). Cyclisations of type (*a*) have been shown to occur readily in the preparation of tetrahydroquinoxalines by a related route (see previous paper). On the other hand, cyclisations of type (*b*) occur in pyridine and quinoline derivatives possessing the 2′-chloroethylamino-group in the 2-position (Bremer, *Annalen*, 1936, **521**, 286; Osbond, *J.*, 1950, 1853). No cases appear to have been investigated in which both types of cyclisation are competing, and the present work has established that the formation of the 5-amino-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine occurs in preference to that of the 5 : 6 : 7 : 8-tetrahydropteridine.

Two main series of compounds were investigated, 2 : 4-dichloro-5-nitropyrimidine and its 6-methyl derivative, readily available from the corresponding 2 : 4-dihydroxypyrimidines by Baddiley and Topham's method (*J.*, 1944, 678), being used as starting materials.

By treatment of 2 : 4-dichloro-6-methyl-5-nitropyrimidine with 2-chloroethylamine hydrochloride in the presence of a suspension of sodium hydrogen carbonate, selective condensation at the 4-chloro-group gave 2-chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (I; R = Me, X = Cl) in good yield. This condensation procedure is essentially that used by Boon, Jones, and Ramage (*loc. cit.*) with glycine ester hydrochloride. 2-Chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (I; R = Me, X = Cl) was stable and showed no ready tendency to cyclisation, involving the pyrimidine nitrogen, to give a glyoxalinopyrimidine derivative.

Reduction of (I; R = Me, X = Cl) was accomplished catalytically in methanolic solution by use of Raney nickel. Without isolation of the intermediate 5-amino-2-chloro-4-2′-chloroethylamino-6-methylpyrimidine (V; R = Me, X = Cl), the methanolic solution after removal of the catalyst was refluxed and cyclisation occurred, giving the hydrochloride of 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)-pyrimidine (VI; R = Me, X = Cl). Reductive dehalogenation of this in presence of palladium on calcium carbonate gave 5-amino-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = Me, X = H). This structure was established by identity with the product obtained by the following unambiguous synthesis. Treatment of 2-chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (I; R = Me, X = Cl) with thiourea gave a thiuronium salt, which on hydrolysis to the 2-mercapto-derivative with sodium hydroxide underwent cyclisation, yielding 1 : 6 : 4′ : 5′-tetrahydro-2-mercapto-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VII). Reduction of (VII) with sodium dithionite gave the amino-compound (VIII), which was desulphurised with Raney nickel to give 5-amino-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = Me, X = H).

Similar cyclisations have occurred on attempted replacement of the 2-chloro-group in (I; R = Me, X = Cl) by other groups. On hydrolysis of the 2-chloro-group with hydrochloric acid, cyclisation occurred simultaneously to give 1 : 6 : 4′ : 5′-tetrahydro-2-hydroxy-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine (IX; X = OH). Similarly, on treatment of (I; R = Me, X = Cl) with anhydrous methanolic ammonia at low temperature, a water-insoluble product was first obtained which was apparently the desired 2-amino-compound. This product, however, cyclised with remarkable ease in the solid state when heated on the water-bath or kept in air, to give the hydrochloride of 2-amino-1 : 6 : 4′ : 5′-tetrahydro-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine (IX; X = NH_2).



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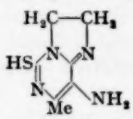

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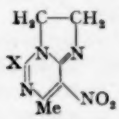


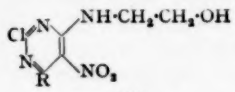
(IX)

The above cyclisations are apparently facilitated by the presence of a group, in the 2-position, capable of undergoing tautomerism, since the intermediate (I; R = Me, X = Cl) was stable, and furthermore, on treatment with piperidine, gave 4-2′-chloroethylamino-6-methyl-5-nitro-2-piperidinopyrimidine (I; R = Me, X = $C_5H_{10}N$) which was also quite stable, there being now no possibility of tautomerism at the 2-position.

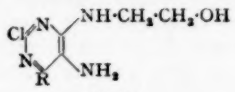
2-Chloro-4-2′-chloroethylamino-5-nitropyrimidine (I; R = H, X = Cl) was prepared from 2 : 4-dichloro-5-nitropyrimidine and 2-chloroethylamine in the same way as its 6-methyl analogue, but its reduction and cyclisation proved to be more difficult. Only about 95% of the theoretical volume of hydrogen was absorbed on catalytic reduction with Raney nickel in methanol at room temperature; the solution thus obtained was extremely sensitive to air, and, when it was refluxed in an atmosphere of carbon dioxide to effect cyclisation, considerable darkening occurred and no satisfactory product could be isolated. By raising the temperature of hydrogenation to 55° after the initial intake of hydrogen had ceased, a further quantity of hydrogen was absorbed, bringing the total intake to that required by theory. The solution thus obtained was far more stable to heat and, when it was refluxed in an atmosphere of carbon dioxide, cyclisation occurred to give the hydrochloride of 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = H, X = Cl), which by reductive dehalogenation gave 5-amino-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = X = H).

Some experiments have also been carried out on the cyclisation of the 4-2′-hydroxyethylamino-5-nitropyrimidines (X; R = H or Me), which were readily prepared by the action of 2-aminoethanol on 2 : 4-dichloro-5-nitropyrimidine and its 6-methyl derivative in methanolic solution at low temperature. A considerable difference in the behaviour of the two nitro-compounds was observed on reduction to the corresponding 5-amino-2-chloro-4-2′-hydroxyethylaminopyrimidines (XI; R = H or Me). 5-Amino-2-chloro-

4-2′-hydroxyethylamino-6-methylpyrimidine (XI; R = Me) was obtained from (X; R = Me) by catalytic reduction with Raney nickel in methanol, in high yield with no appreciable reduction of the 2-chloro-group. On a similar catalytic reduction of (X; R = H) the theoretical 3 mols. of hydrogen were absorbed, but the solution thus produced was extremely sensitive to air and heat. By avoidance of contact with air and removal of methanol under reduced pressure in hydrogen at room temperature, a residue was obtained which by crystallisation gave the more stable, pure 5-amino-2-chloro-4-2′-hydroxyethylaminopyrimidine (XI; R = H). Further differences were observed between the two series in the behaviour of the 5-amino-4-2′-hydroxyethylaminopyrimidines (XI) with hydriodic acid. Treatment of 5-amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine (XI; R = Me) with this acid and red phosphorus resulted in cyclisation and reduction of the 2-chloro-group to give 5-amino-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino-(1′ : 2′-1 : 6)pyrimidine (VI; R = Me, X = H), identical with that produced by cyclisation of the corresponding 4-2′-chloroethylaminopyrimidine (I; R = Me, X = Cl). Hydriodic acid and red phosphorus also directly converted the nitro-compound (X; R = Me) into (VI; R = Me, X = H), reduction of the nitro-group, cyclisation, and removal of the 2-chloro-group all occurring in the one treatment.



(X)



(XI)

Attempts to prepare 5-amino-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = X = H) by the hydriodic acid treatment of 5-amino-2-chloro-4-2′-hydroxyethylaminopyrimidine (XI; R = H) or the corresponding nitro-compound (X; R = H) were unsuccessful owing to hydrolytic fission. The cleavage was evident from the isolation of ethylenediamine as its dibenzoyl derivative after hydriodic acid treatment of (XI; R = H) and the isolation of oxazolid-2-one after similar treatment of (X; R = H). Oxazolid-2-one was apparently formed from the hydrolytic fission product 2-iodoethylamine, since, in the working up, the reaction mixture was made alkaline with potassium carbonate and evaporated to dryness, and oxazolid-2-one has been prepared by the action of sodium hydrogen carbonate on 2-bromoethylamine under mild conditions (Gabriel and Eschenbach, *Ber.*, 1897, **30**, 2494).

Substitution of hydrochloric acid (at 140—150°) for the cyclisation of 5-amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine (XI; R = Me), which might be expected to give 5-amino-1 : 6 : 4′ : 5′-tetrahydro-2-hydroxy-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = Me, X = OH), caused fission with the production of 5-amino-4-methyluracil.

The 5-amino-4-2′-hydroxyethylaminopyrimidines (XI; R = H or Me) were also cyclised by conversion with thionyl chloride into the corresponding 5-amino-2-chloro-4-2′-chloroethylaminopyrimidines (V; R = H or Me, X = Cl), which were cyclised in refluxing methanol to the appropriate 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino-(1′ : 2′-1 : 6)pyrimidines (VI; R = H or Me, X = Cl). Yields were low, however, and these compounds are far better prepared by the reduction and cyclisation of the 2-chloro-4-2′-chloroethylamino-5-nitropyrimidines (I; R = H or Me, X = Cl).

Experimental

Analyses by Drs. Weiler and Strauss, Oxford.

2-Chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (I; R = Me, X = Cl).—2-Chloroethylamine hydrochloride (14 g., 0·12 mol.) was added with shaking during 20 minutes to 2 : 4-dichloro-6-methyl-5-nitropyrimidine (20·8 g., 0·1 mol.) in ether (100 c.c.) in the presence of sodium hydrogen carbonate (24 g.) in water (100 c.c.), at room temperature. After the addition, shaking was continued for a further 40 minutes before the ethereal layer was separated and the aqueous layer extracted with ether. The combined ethereal solutions were washed once with water and dried (Na_2SO_4). The residue, after removal of ether, was an oil which readily solidified on cooling and was crystallised from *cyclo*hexane (charcoal), to

give *2-chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine* (18·2 g., 72%) as massive, pale yellow needles, m. p. 62—63° (Found: C, 33·7; H, 3·4; Cl, 28·2. $C_7H_8O_2N_4Cl_2$ requires C, 33·5; H, 3·2; Cl, 28·2%).

2-Chloro-4-2′-hydroxyethylamino-6-methyl-5-nitropyrimidine (X; R = Me).—A solution of 2-aminoethanol (12·2 g., 0·2 mol.) in methanol (50 c.c.) was added slowly (20 minutes) with shaking to a solution of 2 : 4-dichloro-6-methyl-5-nitropyrimidine (20·8 g., 0·1 mol.) in methanol (60 c.c.) in a freezing mixture. During the addition the product began to separate and, after a further 2 hours in the freezing mixture, was filtered off and washed with a little methanol. Crystallisation from methanol gave *2-chloro-4-2′-hydroxyethylamino-6-methyl-5-nitropyrimidine* (18·6 g., 80%), in pale yellow needles, m. p. 131° (Found: C, 36·3; H, 3·7. $C_7H_9O_3N_4Cl$ requires C, 36·1; H, 3·9%).

5-Amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine (XI; R = Me).—2-Chloro-4-2′-hydroxyethylamino-6-methyl-5-nitropyrimidine (5 g.) was suspended in methanol (60 c.c.) and shaken with Raney nickel (3 c.c.; settled suspension) in hydrogen until the intake of hydrogen (theoretical amount) ceased (about 1½ hours). The catalyst was filtered off and washed with methanol, and the solvent removed from the filtrate under reduced pressure at 60°. Crystallisation of the residue from water gave *5-amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine* (3·77 g., 86%) as buff-coloured needles, m. p. 177—178° (Found: C, 41·2; H, 5·3; N, 28·2. $C_7H_{11}ON_4Cl$ requires C, 41·5; H, 5·5; N, 27·7%).

5-Amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = Me, X = Cl).—(*a*) 2-Chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (2 g.) in ethanol (100 c.c.) was shaken in hydrogen at room temperature and atmospheric pressure, in the presence of Raney nickel catalyst (4 c.c.; settled suspension) until the theoretical 3 mols. of hydrogen were absorbed. After filtration the filtrate was refluxed for 2½ hours, then concentrated to small bulk. The *hydrochloride* of the base (VI; R = Me, X = Cl) (1·44 g.) separated and crystallised from 90% aqueous ethanol as short needles which did not melt below 300° (Found: C, 38·5; H, 4·7; Cl, 32·0. $C_7H_9N_4Cl,HCl$ requires C, 38·0; H, 4·6; Cl, 32·1%). The free *base* was precipitated from an aqueous solution of the hydrochloride with concentrated sodium hydroxide solution, and after crystallisation from water and drying in a vacuum was obtained as needles, m. p. 163° (Found: C, 45·9; H, 5·2. $C_7H_9N_4Cl$ requires C, 45·5; H, 4·9%).

(*b*) 5-Amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine (4 g.) was added gradually (10 minutes) to thionyl chloride (10 c.c.) at 40°. The mixture was kept at 40° for a further 1½ hours, and the excess of thionyl chloride then removed under reduced pressure. The residue was treated with ice-water (50 c.c.), made alkaline with solid potassium carbonate, and extracted with chloroform. The extracts were dried (Na_2SO_4) and taken to dryness under reduced pressure below 40°, and the residue was dissolved in ethanol (200 c.c.) and refluxed for 2½ hours. Some hydrochloride which had separated during refluxing was taken into solution by addition of water (20 c.c.), and the hot solution treated with charcoal and filtered. Evaporation of the filtrate to dryness and crystallisation of the residue from 90% aqueous ethanol gave the hydrochloride of 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)-pyrimidine (2·41 g.), identical with that obtained above.

1 : 6 : 4′ : 5′-Tetrahydro-2-mercapto-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VII).—Thiourea (1·67 g., 0·022 mol.) in acetone (60 c.c.) was added to 2-chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (5 g., 0·02 mol.) in acetone (20 c.c.), and the mixture kept overnight and then refluxed for 2 hours. The thiuronium salt (6·05 g.) which separated was filtered off and dissolved in N-sodium hydroxide (120 c.c.) by warming on the water-bath for 2—3 minutes. The alkaline solution was cooled and acidified with glacial acetic acid, to precipitate the *compound* (VII) (3·55 g., 84%). The material was purified for analysis by twice precipitating it with acetic acid from a large volume of 0·1N-sodium hydroxide (120 c.c., to 1 g. of thio-compound) followed by crystallisation from 2-ethoxyethanol, to give orange prisms, m. p. 270° (decomp.) (Found: C, 40·1; H, 4·0. $C_7H_8O_2N_4S$ requires C, 39·6; H, 3·8%).

5-Amino-1 : 6 : 4′ : 5′-tetrahydro-2-mercapto-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (VIII).—The above nitro-compound (2 g.) was suspended in aqueous ammonia (30 c.c.; *d* 0·88), sodium dithionite (12 g.) was added during about 5 minutes, and the mixture was carefully heated to boiling. After cooling, the product was filtered off and crystallised from water containing a little sodium dithionite and ammonia, to give *5-amino-1 : 6 : 4′ : 5′-tetrahydro-2-mercapto-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine* (1·2 g., 71%) as colourless prisms, m. p. 300° (decomp.) (Found: C, 45·9; H, 5·7; S, 17·7. $C_7H_{10}N_4S$ requires C, 46·1; H, 5·5; S, 17·6%).

5-Amino-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = Me, X = H).—(*a*) A suspension of 5-amino-1 : 6 : 4′ : 5′-tetrahydro-2-mercapto-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (1 g.) and Raney nickel (15 c.c.; settled suspension) in ethanol (20 c.c.) was refluxed for 6 hours. The Raney nickel was removed by filtration and washed with a little ethanol, and the combined filtrates taken to dryness. The residue was crystallised from moist ethyl acetate, to give the *dihydrate* of the base (VI; R = Me, X = H) (0·25 g.) as buff-coloured needles, m. p. 108° (Found: C, 45·1; H, 7·4. $C_7H_{10}N_4,2H_2O$ requires C, 45·1; H, 7·6%). When the dihydrate was dried *in vacuo* at 65° the anhydrous base, m. p. 155°, was obtained, but its analyses were not satisfactory since it is hygroscopic and reverts to the dihydrate in air overnight. The *hydriodide* crystallised from water as prisms, m. p. 265° (decomp.) (Found: C, 30·3; H, 4·0; N, 20·4; I, 45·6. $C_7H_{10}N_4,HI$ requires C, 30·2; H, 4·0; N, 20·2; I, 45·6%). The *picrate* was sparingly soluble in ethanol and crystallised from 2-ethoxyethanol as tablets, m. p. 244° (decomp.) (Found: N, 25·6. $C_7H_{10}N_4,C_6H_3O_7N_3$ requires N, 25·9%).

(*b*) 5-Amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine (1 g.) in methanol (30 c.c.) was shaken in hydrogen in the presence of palladium on calcium carbonate (2%; 0·5 g.) at room temperature and pressure. When the intake of hydrogen ceased the catalyst was filtered off and the methanolic solution taken to dryness. The residual hydrochloride was dissolved in a little water, and 5-amino-1 : 6 : 4′ : 5′-tetrahydro-4-methylglyoxalino(1′ : 2′-1 : 6)pyrimidine precipitated with concentrated sodium hydroxide solution. Crystallisation from moist ethyl acetate gave the dihydrate (0·7 g.), m. p. 108°, identical with that obtained above.

(*c*) 5-Amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine (2 g.) was added to hydriodic acid (10 c.c.; *d* 1·7) and red phosphorus (0·5 g.). After refluxing for 1½ hours the mixture was taken to dryness on the water-bath under reduced pressure, and the residue dissolved in a little hot water and filtered from excess of red phosphorus. The aqueous solution was evaporated to dryness, the residual hydriodide dissolved in hot water (4 c.c.), and the free base precipitated by making the solution alkaline with sodium hydroxide solution (30%), cooling, and then making it strongly alkaline by the further addition of sodium hydroxide. Crystallisation from moist ethyl acetate gave the above dihydrate (1·36 g.), m. p. 108°.

(*d*) 2-Chloro-4-2′-hydroxyethylamino-6-methyl-5-nitropyrimidine (4 g.), hydriodic acid (20 c.c.; *d* 1·7), and red phosphorus (2 g.) were refluxed for 1½ hours, the excess of red phosphorus filtered off, and the filtrate taken to dryness on the water-bath under reduced pressure. The residue was treated with water (10 c.c.), and the resultant suspension made strongly alkaline with sodium hydroxide solution (60%). The precipitate thus obtained was filtered off and dried in a desiccator, and contained inorganic material. The dry mixture was extracted (Soxhlet) with ethyl acetate (150 c.c.) for 6 hours, and when the extracts were cooled the dihydrate (1·26 g.), m. p. 108°, separated.

1 : 6 : 4′ : 5′-Tetrahydro-2-hydroxy-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine (IX; X = OH).—2-Chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (2 g.) was refluxed for 15 minutes with hydrochloric acid (5N; 20 c.c.). On cooling, a hydrochloride crystallised and was filtered off. This (1·4 g.) was dissolved in a little hot water, and the free base precipitated with sodium hydrogen carbonate. Crystallisation from water gave 1 : 6 : 4′ : 5′-*tetrahydro-2-hydroxy-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine* as broad needles, m. p. 286° (decomp.) (Found: C, 43·0; H, 4·1. $C_7H_8O_3N_4$ requires C, 42·9; H, 4·1%).

2-Amino-1 : 6 : 4′ : 5′-tetrahydro-4-methyl-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine (IX; X = NH_2).—Methanolic ammonia (2·6N; 5 c.c.) was added to a solution of 2-chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (1·25 g.) in methanol (5 c.c.). After the mixture had been kept for 1 hour at room temperature and then for 30 minutes in the refrigerator, some solid material separated and was filtered off and washed with water. The water-insoluble residue (0·3 g.) was converted into a water-soluble hydrochloride on drying either by heating it on the water-bath or keeping it in air. The free *base* (IX; X = NH_2) was precipitated from a solution of this hydrochloride with sodium hydrogen carbonate and crystallised from water in orange-coloured needles which did not melt below 300° (Found: C, 43·4; H, 4·6. $C_7H_9O_2N_5$ requires C, 43·1; H, 4·6%).

4-2′-Chloroethylamino-4-methyl-5-nitro-2-piperidinopyrimidine (I; R = Me, X = $C_5H_{10}N$).—Piperidine (0·85 g., 0·01 mol.) in methanol (4 c.c.) was added gradually with shaking to 2-chloro-4-2′-chloroethylamino-6-methyl-5-nitropyrimidine (1·25 g., 0·005 mol.) in methanol (4 c.c.) in an ice-bath. *4-2′-Chloroethylamino-4-methyl-5-nitro-2-piperidinopyrimidine* separated immediately and after 30 minutes was filtered off and washed with a little methanol (1·4 g., 93%;

m. p. 103—104°). Crystallisation from methanol gave pale yellow needles, m. p. 104—105° (Found: C, 48·5; H, 5·9. $C_{12}H_{18}O_2N_5Cl$ requires C, 48·1; H, 6·1%).

2-Chloro-4-2′-chloroethylamino-5-nitropyrimidine (I; R = H, X = Cl).—2 : 4-Dichloro-5-nitropyrimidine (19·4 g.) in ether (150 c.c.) and 2-chloroethylamine hydrochloride (14 g.) together with sodium hydrogen carbonate (24 g.) in water (100 c.c.), in a similar manner to its 6-methyl analogue above, gave *2-chloro-4-2′-chloroethylamino-5-nitropyrimidine* (17·2 g.), which crystallised from *cyclo*hexane containing a little ethyl acetate as pale yellow prisms, m. p. 75° (Found: C, 30·3; H, 2·4; Cl, 29·5. $C_6H_6O_2N_4Cl_2$ requires C, 30·4; H, 2·6; Cl, 29·9%).

2-Chloro-4-2′-hydroxyethylamino-5-nitropyrimidine (X; R = H).—2 : 4-Dichloro-5-nitropyrimidine (19·4 g.) in methanol (60 c.c.) was treated with 2-aminoethanol (12·2 g.) in methanol (50 c.c.) as described for the 6-methyl derivative. The resulting *compound* (X; R = H) (16·2 g.) crystallised from methanol in pale yellow needles, m. p. 125° (Found: C, 32·9; H, 3·3. $C_6H_7O_3N_4Cl$ requires C, 33·0; H, 3·2%).

5-Amino-2-chloro-4-2′-hydroxyethylaminopyrimidine (XI; R = H).—The compound (X; R = H) (5 g.) was suspended in methanol (100 c.c.) and shaken with Raney nickel (3 c.c.; settled suspension) until the theoretical volume of hydrogen was absorbed. The catalyst was filtered off and washed with methanol, contact with air being reduced to a minimum. The filtrate was evaporated to dryness under reduced pressure, in an atmosphere of hydrogen, at room temperature. The residual gum slowly crystallised and was recrystallised from nitromethane (charcoal) from which the product separated as a light brown solid (3·03 g., 70%), m. p. 144—145·5°. Recrystallisation from water gave pure *5-amino-2-chloro-4-2′-hydroxyethylaminopyrimidine* as buff-coloured needles, m. p. 152—153° (Found: C, 38·3; H, 4·9; N, 29·8. $C_6H_9ON_4Cl$ requires C, 38·2; H, 4·8; N, 29·7%).

5-Amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = H, X = Cl).—(*a*) A solution of 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine (4 g.) in methanol (50 c.c.) was shaken with hydrogen in the presence of Raney nickel catalyst (12 c.c.; settled suspension) at room temperature and pressure. After the initial intake of hydrogen had ceased, the temperature was raised to 55° until the intake again ceased (total, 1200 c.c. at N.T.P.; theory, 1180 c.c.). The catalyst was removed by filtration, and the filtrate diluted to 100 c.c. with methanol and refluxed for 2½ hours in an atmosphere of carbon dioxide. On concentration to about 15 c.c. the *hydrochloride* of 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino-(1′ : 2′-1 : 6)pyrimidine (2·35 g.) separated, and crystallised from aqueous ethanol in needles not melting below 300° (Found: C, 35·1; H, 3·8. $C_6H_7N_4Cl,HCl$ requires C, 34·8; H, 3·9%). The free *base* was precipitated from an aqueous solution and crystallised from ethyl acetate as needles, m. p. 157° (Found: C, 42·8; H, 3·8. $C_6H_7N_4Cl$ requires C, 42·2; H, 4·1%).

(*b*) 5-Amino-2-chloro-4-2′-hydroxyethylaminopyrimidine (2 g.) was added during 10 minutes to thionyl chloride (12 c.c.) at room temperature, and the resulting mixture warmed on the water-bath for 15 minutes. Excess of thionyl chloride was removed under reduced pressure at 40°, and the residue dissolved in ice-water (30 c.c.). The aqueous solution was made alkaline with solid potassium carbonate and extracted with chloroform. After the extracts had been dried (Na_2SO_4), the chloroform was removed under reduced pressure, and the gummy residue dissolved in ethanol (50 c.c.) and refluxed for 2½ hours. Some hydrochloride which separated was taken into solution by addition of a little water, and the hot solution was treated with charcoal and filtered. On concentration of the filtrate to about 10 c.c., the above hydrochloride of 5-amino-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (0·58 g.) separated.

5-Amino-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (VI; R = X = H).—Anhydrous 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine (1 g) in methanol (25 c.c.) was shaken in hydrogen with palladium on calcium carbonate (2%; 0·5 g.). When the intake of hydrogen ceased, the catalyst was filtered off and the methanolic solution taken to dryness under reduced pressure. The residual hydrochloride was treated with 1 mol. of methanolic sodium methoxide, and the sodium chloride which separated was filtered off. The filtrate was taken to dryness, and crystallisation of the residue from moist ethyl acetate gave the base (VI; R = X = H) (0·58 g.) as a hydrate, m. p. 71°. On drying in a vacuum-desiccator the anhydrous *base*, m. p. 140°, was obtained (Found: C, 53·3; H, 5·9. $C_6H_8N_4$ requires C, 52·9; H, 5·9%). The *picrate* was sparingly soluble in alcohol and crystallised from 2-ethoxyethanol; it had m. p. 240° (decomp.) (Found: C, 40·1; H, 3·1. $C_{12}H_{11}O_7N_7$ requires C, 39·5; H, 3·0%).

Hydriodic Acid Treatment of 5-Amino-2-chloro-4-2′-hydroxyethylaminopyrimidine (XI; R = H).—5-Amino-2-chloro-4-2′-hydroxyethylaminopyrimidine (1 g.), hydriodic acid (10 c.c.; *d* 1·7), and red phosphorus (0·5 g.) were refluxed together for 1 hour. Excess of hydriodic

acid was removed on the water-bath under reduced pressure, the residue treated with water (10 c.c.), and excess of red phosphorus filtered off. After evaporation of the clarified solution to dryness, the residue was washed with hot ethanol (10 c.c.), and an ethanol-insoluble hydriodide (0·55 g.) remained. Shaking this hydriodide with benzoyl chloride (1·3 c.c.) and 5% sodium hydroxide solution (20 c.c.) for 1 hour yielded a benzoyl derivative (0·23 g.) which was filtered off. After crystallisation from ethanol it had m. p. 251° and was shown by analysis to be the dibenzoyl derivative of ethylenediamine (Found: C, 71·2; H, 6·0. Calc. for $C_{16}H_{16}O_2N_2$: C, 71·6; H, 6·0%). The m. p. was not depressed on admixture with an authentic specimen, m. p. 251°.

Hydriodic Acid Treatment of 2-Chloro-4-2′-hydroxyethylamino-5-nitropyrimidine (X; R = H).—The nitropyrimidine (2 g.) was added to a mixture of hydriodic acid (10 c.c.; *d* 1·7) and red phosphorus (1 g.). After 1 hour's refluxing, the excess of red phosphorus was removed by filtration, and the filtrate taken to dryness on the water-bath under reduced pressure and again after being made alkaline with aqueous potassium carbonate. The residual mixture was extracted with ethanol (2 × 100 c.c.) and after concentration of the extract to about 20 c.c. it was diluted with an equal volume of benzene and filtered. The filtrate was taken to dryness, and the residue sublimed at 90—120°/0·01 mm., to yield a colourless sublimate (0·28 g.), m. p. 77—84°. Crystallisation from alcohol gave colourless needles, m. p. 89—90°, of oxazolid-2-one (lit., m. p. 90—91°) (Found: C, 42·0; H, 5·6. Calc. for $C_3H_5O_2N$: C, 41·4; H, 5·8%).

Hydrochloric Acid Treatment of 5-Amino-2-chloro-4-2′-hydroxyethylamino-6-methylpyrimidine (X; R = Me).—This base (2 g.) was heated (sealed tube) with concentrated hydrochloric acid (10 c.c.) at 140° for 6 hours. On cooling, a highly crystalline hydrochloride separated (1·35 g.), which after filtration was dissolved in hot water and treated with solid sodium hydrogen carbonate to liberate the base. After crystallisation from water this had m. p. 270° (decomp.) with softening at about 250°, and was identical with 5-amino-4-methyluracil obtained by reduction of 4-methyl-5-nitrouracil with sodium dithionite (Bogert and Davidson, *J. Amer. Chem. Soc.*, 1933, **55**, 1667). It was dried for analysis at 100° *in vacuo* (Found: C, 42·9; H, 4·7. Calc. for $C_5H_7O_2N_3$: C, 42·5; H, 5·0%).

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The Technical College, Huddersfield. [*Received, August 6th*, 1952.]

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847. *Tropolones. Part VI.* Further Reactions of Tropolone.*

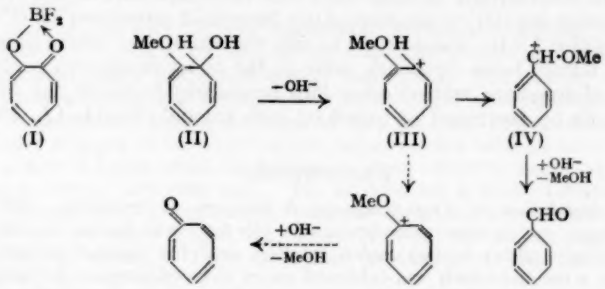
By J. W. Cook, R. A. Raphael, and A. I. Scott.

The Friedel–Crafts, Gattermann, Kolbe–Schmidt, and chloromethylation reactions failed to give substitution products with tropolone. The Reimer–Tiemann reaction, however, gave a small yield of γ-formyltropolone. Lithium aluminium hydride reduction of tropolone led to traces of *cyclo*hept-4-ene-1 : 2-dione, but tropolone methyl ether was converted into benzaldehyde by this reagent.

The somewhat close parallel between the reactions of tropolone and of phenol (*e.g.*, halogenation, nitration, diazo-coupling) suggested investigation of the behaviour of tropolone in other electrophilic substitution reactions. *iso*Propylation of tropolone under Friedel–Crafts conditions was first attempted as all three possible monosubstitution products (the thujaplicins) were known. Treatment of tropolone in *iso*propyl chloride solution with aluminium chloride furnished a complex from which tropolone was regenerated by acid treatment. In an attempt to circumvent this difficulty tropolone methyl ether was similarly treated but tropolone was again recovered. *C*-Acetylation was attempted by using acetyl chloride and aluminium chloride, but once more tropolone was the sole isolable

* Part V, *J.*, 1952, 2350.

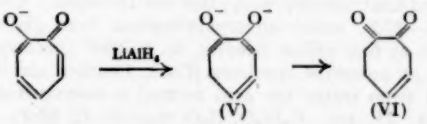
material. Similar results were obtained with acetic anhydride–stannic chloride and acetic anhydride–phosphoric acid, the latter reagents furnishing some *O*-acetyltropolone. Heating tropolone with a solution of boron trifluoride in acetic acid produced a complex to which structure (I) may be assigned. Analogous products have been obtained from both *o*-acylphenols and β-diketones, the chelate ring in these compounds being six-membered (Hauser and Man, *J. Org. Chem.*, 1952, **17**, 393; Kästner, " Newer Methods of Preparative Organic Chemistry," Interscience Publ., New York, 1948, pp. 282, 287). An obvious contributory factor to the failure of these substitution reactions is the ready co-ordination of the strongly electron-donating tropolone with the Lewis acid type of catalyst involved.



Tropolone was also recovered unchanged after being subjected to the Gattermann reaction with zinc cyanide and hydrogen chloride. Attempted chloromethylation, with either paraformaldehyde or chloromethyl methyl ether, gave only tropolone hydrochloride. Three procedures for the Kolbe–Schmidt carboxylation reaction led to recovery of the tropolone.

More success followed when tropolone was subjected to the Reimer–Tiemann reaction; heating with sodium hydroxide and chloroform gave a small yield of γ-formyltropolone the structure of which was established by oxidation to tropolone-γ-carboxylic acid, prepared by Mr. D. K. V. Steel in this laboratory by a method which established the structure. This acid was obtained directly when carbon tetrachloride was employed in place of chloroform. An attempt to prepare the aldehyde by using the *N*-methylformanilide–phosphorus oxychloride procedure was unsuccessful.

In Part I (*J.*, 1951, 503) brief mention was made of the lithium aluminium hydride reduction of tropolone. Careful repetition of this work showed that the primary product rapidly resinified when the reaction mixture was hydrolysed. Distillation of the resulting tar gave a very small yield of a liquid which readily gave a bis-2 : 4-dinitrophenylhydrazone. The ultra-violet absorption curve of this derivative resembled very closely that of the bis-2 : 4-dinitrophenylhydrazone of *cyclo*heptane-1 : 2-dione although the two compounds were clearly different. It is suggested, therefore, that the liquid reduction product was *cyclo*hept-4-ene-1 : 2-dione (VI) produced by 1 : 4- or 1 : 6-addition of lithium aluminium hydride to the dienone system of the initially formed lithium tropolone derivative; hydrolysis of the resulting dienolate (V) would give the dione (VI) by ketonisation:



A similar mechanism has been proposed to account for the production of 3-hydroxy-1 : 4-diphenylbutan-1-one by reduction of dibenzoylethylene (Lutz and Gillespie, *J. Amer. Chem. Soc.*, 1950, **72**, 2002; cf. Cavalla and McGhie, *J.*, 1951, 834).

It is of interest that the two bis-2 : 4-dinitrophenylhydrazones mentioned above exhibit a maximal absorption in the ultra-violet (3560 Å) which corresponds to that of

an unconjugated mono-derivative (cf. Braude and Jones, *J.*, 1945, 498). This must mean that the two hydrazone groupings are so far from possessing the coplanar configuration necessary for complete conjugation that they behave as discrete chromophores. This result is in harmony with the observation that the planes of the carbonyl groups of 3 : 3 : 7 : 7-tetramethyl*cyclo*heptane-1 : 2-dione are inclined at right angles (Leonard and Mader, *J. Amer. Chem. Soc.*, 1950, **72**, 5388).

Reduction of tropolone methyl ether with lithium aluminium hydride gave a completely different and surprising result, for a substantial yield of benzaldehyde was obtained. This may be explained by postulating that the primary reduction product (II) undergoes anionotropy with concomitant Wagner–Meerwein rearrangement of the resulting seven-membered carbonium ion (III) to the more stable benzenoid carbonium ion (IV). Although it would seem feasible for the anionotropy to take the alternative course shown to produce *cyclo*hepta-2 : 4 : 6-trien-1-one (tropone), none of the latter compound could be isolated. The conversion of tropolone methyl ether into benzaldehyde recalls the formation of *o*-chlorobenzaldehyde by treatment of tropolone with thionyl chloride (*J.*, 1952, 2350).

Experimental

Attempted C-Acetylation of Tropolone.—(*a*) A mixture of tropolone (200 mg.), acetic anhydride (200 mg.), and syrupy phosphoric acid (40 mg.) was heated at 110° for 3 hours. Water was cautiously added to the cooled solution, and the product isolated with ether. Evaporation gave a residue which was sublimed under reduced pressure to yield (i) tropolone (110 mg.) and (ii) an oil, b. p. 80° (bath-temp.)/10 mm. The latter soon solidified and crystallised from light petroleum (b. p. 60—80°) to give *O*-acetyltropolone (60 mg.) as prisms, m. p. 67° (Kofler block) (Found: C, 65·1; H, 5·0. Calc. for $C_9H_8O_3$: C, 65·6; H, 4·9%). (*b*) Tropolone (150 mg.) was dissolved in glacial acetic acid (1 c.c.) and boron trifluoride–ether (1 c.c.) added; an immediate precipitation occurred. The mixture was heated in a sealed tube at 70° for 5 hours, and, after cooling, the crystalline precipitate was filtered off. Crystallisation from acetic acid or light petroleum (b. p. 100—120°) yielded the *complex* (I) (110 mg.) as large plates, m. p. 151° (Found: C, 49·7; H, 3·3. $C_7H_5O_2F_2B$ requires C, 49·5; H, 2·95%). The complex gave no colour with ferric chloride but was hydrolysed to tropolone with boiling dilute sulphuric acid. Use of aluminium chloride or stannic chloride as catalyst led to recovery of the tropolone.

Reimer–Tiemann Reaction.—A mixture of tropolone (500 mg.), water (12 c.c.), and 10N-sodium hydroxide solution (4 c.c.) was warmed until solution was complete, and chloroform (0·5 c.c.) was then added. The resulting dark red solution was heated by steam and a further quantity of chloroform (1 c.c.) added during 1 hour. After a further 2 hours' heating the cooled mixture was acidified to Congo-red with dilute sulphuric acid, and an amorphous brown precipitate (50 mg.), m. p. >300°, filtered off. The filtrate was extracted continuously with ether for 24 hours. Drying (Na_2SO_4) and removal of solvent furnished a yellow gum which, on being fractionally sublimed under reduced pressure, gave tropolone (100—200 mg.), subliming at 60—80° (bath-temp.)/18 mm., and a yellow solid (20—25 mg.), subliming at 100—120° (bath-temp.)/18 mm. Repeated crystallisation of the latter product from ethanol gave *γ-formyltropolone* as bright yellow needles, m. p. 181° (decomp.), which slowly decomposed on exposure to light (Found: C, 64·0; H, 4·2. $C_8H_6O_3$ requires C, 64·0; H, 4·0%).

Tropolone-γ-carboxylic Acid.—(*a*) γ-Formyltropolone (24 mg.) was added to a suspension of freshly precipitated silver oxide (68 mg.) in 4N-sodium hydroxide solution (0·5 c.c.), and the mixture heated by steam for 30 minutes. The cooled, filtered solution was acidified with dilute sulphuric acid and extracted continuously with ether for 16 hours. Evaporation gave a yellow solid (12 mg.), m. p. 250—270°, which on crystallisation from glacial acetic acid afforded tropolone-γ-carboxylic acid as fine yellow needles, m. p. 288° (decomp.; sealed tube), undepressed on admixture with an authentic specimen (Cook, Loudon, and Steel, future communication). When crystallised from water the acid formed a *monohydrate*, yellow prisms, m. p. 222—225° (Found: C, 52·1; H, 4·4. $C_8H_6O_4,H_2O$ requires C, 52·2; H, 4·3%). Treatment of the acid with ethereal diazomethane gave the corresponding methyl ether methyl ester which crystallised from benzene as fine white needles; m. p. and mixed m. p. 184·5°.

(*b*) A mixture of tropolone (100 mg.), potassium hydroxide (300 mg.), ethanol (0·5 c.c.), water (0·5 c.c.), and carbon tetrachloride (100 mg.) was heated at 100° in a sealed tube for 16 hours. Cooling and acidification followed by continuous ether-extraction and fractional sublimation gave tropolone (60 mg.) and a pale yellow solid subliming at 180° (bath-temp.)/0·4

mm. Crystallisation of this latter from water gave tropolone-γ-carboxylic acid hydrate (3 mg.), m. p. and mixed m. p. 222—225°.

Attempted Reaction with N-*Methylformanilide.*—A mixture of tropolone (200 mg.), *N*-methylformanilide (550 mg.), and phosphorus oxychloride (500 mg.) was kept at room temperature for 16 hours. The product was poured into water and extracted with ether. The extract was then shaken out with 1% sodium hydroxide solution; acidification and ether-extraction furnished tropolone (100 mg.). In one experiment evaporation of the alkali-washed extract gave an oil possessing carbonyl activity which gave a 2 : 4-*dinitrophenylhydrazone*, scarlet needles, m. p. 206° (from butanol), having the composition of the derivative of a formyltropolone (Found : C, 50·8; H, 3·0. $C_{14}H_{10}O_6N_4$ requires C, 50·9; H, 3·0%). This result could not be repeated, however.

Reduction of Tropolone with Lithium Aluminium Hydride.—A solution of tropolone (900 mg.) in dry ether (5 c.c.) was added to a slurry of lithium aluminium hydride (1 g.) in ether (40 c.c.). The initial yellow precipitate rapidly redissolved. The mixture was heated under reflux for 30 minutes, cooled, and decomposed with ice-cold dilute sulphuric acid. The initial yellow colour of the solution rapidly darkened to deep red; this could not be prevented either by working under nitrogen or carrying out the decomposition with ice alone. Isolation with ether yielded a dark red gum which on distillation at 80—100°/18 mm. gave a pale yellow oil (100 mg.) and a brown resin (600 mg.). The oil afforded a *bis*-2 : 4-*dinitrophenylhydrazone* which, after chromatographic purification (benzene–alumina), crystallised from benzene in red prisms, m. p. 183—185° (Found : C, 47·5; H, 3·35; N, 23·15. $C_{19}H_{16}O_8N_8$ requires C, 47·1; H, 3·35; N, 23·15%). Light absorption in chloroform : Max. at 3560 Å (ε = 36,500), inflexion at 3960 Å (ε = 29,000).

The *bis*-2 : 4-*dinitrophenylhydrazone* of *cyclo*heptane-1 : 2-dione, after chromatographic purification (benzene–alumina) crystallised from benzene as red needles which contained benzene of crystallisation (Found : C, 53·8; H, 4·4; N, 20·1. $C_{19}H_{18}O_8N_8,C_6H_6$ requires C, 53·2; H, 4·3; N, 19·85%). Drying at 140°/18 mm. gave the solvent-free *compound*, m. p. 213° (Found : C, 47·55; H, 4·1; N, 22·65. $C_{19}H_{18}O_8N_8$ requires C, 46·9; H, 3·75; N, 23·0%). Light absorption in chloroform : Max. at 3520 Å (ε = 34,000), inflexion at 3900 Å (ε = 27,500).

Reduction of Tropolone Methyl Ether with Lithium Aluminium Hydride.—A solution of anhydrous tropolone methyl ether (1 g.) was added to lithium aluminium hydride (1 g.) in ether (20 c.c.). After the initial vigorous reaction heating was continued for 30 minutes and the mixture then decomposed with ice. Ether-extraction gave an oil smelling strongly of benzaldehyde. Treatment of the product with excess of ethanolic 2 : 4-dinitrophenylhydrazine sulphate gave a derivative which was washed and dried. The product (0·9 g.; m. p. *ca.* 200°) was purified by chromatography (benzene–alumina), yielding benzaldehyde 2 : 4-dinitrophenylhydrazone, m. p. 236° undepressed on admixture with an authentic sample. The filtrate from the preparation of the derivative was neutralised with ammonia and several times extracted with ether. Evaporation gave a minute amount of yellow oil which did not give a picrate or hydrochloride.

One of us (A. I. S.) gratefully acknowledges a Maintenance Allowance from the Department of Scientific and Industrial Research.

THE UNIVERSITY OF GLASGOW. [*Received, July 3rd,* 1952.]

848. *Carveol and Related Substances.*

By A. Blumann and W. R. Wood.

Optically active *cis*- and *trans*-carveol are readily racemised by acid. The carveol from autoxidised (+)-limonene is mainly the (±)-*trans*-epimer. It is also formed by thermal decomposition of *trans*-sobreryl acetate, and on hydration it forms (±)-*trans*-sobrerol.

Thermal decomposition of the acetate of *cis*-*p*-menth-8-ene-1 : 2-diol gives (±)-*trans*-carveol accompanied by an isomer which is probably *p*-mentha-1(7) : 8-dien-2-ol.

(±)-*cis*-Carveol is formed by thermal decomposition of the acetate of (±)-*p*-menthane-1 : 2 : 8-triol and on hydration it forms *cis*-sobrerol, which, however, changes slowly into the *trans*-form.

Carveol, first isolated from the products of autoxidation of (+)-limonene in a racemic form (Blumann and Zeitschel, *Ber.*, 1914, **47**, 2624) and later prepared by Ponndorf (*Z. angew. Chem.*, 1926, **39**, 138) by reduction of (+)-carvone with aluminium *iso*propoxide, was considered uniform till Johnston and Read (*J.*, 1934, 233) proved that Ponndorf's product was a mixture of (+)-*cis*- and (+)-*trans*-carveol. It has now been shown that this mixture is readily racemised by cold sulphuric acid in ether and that, with phthalic anhydride, it forms mainly (±)-*trans*-carveyl hydrogen phthalate.

The identity of the carveol from autoxidised limonene with (±)-*trans*-carveol has also been proved by preparation of its 3 : 5-dinitrobenzoate. It is remarkable that the bulk of this carveol is no longer optically active, and Wallach (*Annalen*, 1891, **281**, 132) was puzzled by the fact that he obtained (±)-carvone by oxidation of the active carveyl methyl ether which he prepared from (+)-1 : 2 : 8-tribromo-*p*-menthane. Our experiments indicate that it is not the carvone which is racemised by acid, but the carveol, *cis* as well as *trans*, since acetic and phthalic anhydrides at elevated temperatures and sulphuric acid in ether at low temperatures, and even the mild acids produced during autoxidation, readily induce racemisation.

It was found by Blumann and Zeitschel (*loc. cit.*) that carveol, when hydrated with dilute sulphuric acid, yielded a diol, the constitution of which was not then determined. It was suggested (Beilstein, 4th edn., 1st Suppl., **6**, 377) that this diol is identical with (±)-sobrerol, and this has now been demonstrated by mixed m. p. with an authentic sample. We consider it to be the *trans*-form, although Wagner (*Ber.*, 1899, **32**, 2088) claimed that it was the *cis*-. We have also prepared it from the mixture of (−)-carveols prepared by Ponndorf reduction, but we could not isolate the corresponding *cis*-sobrerol in this case as it appears to form pinol with greater ease than the *trans*-epimer. (±)-*cis*-Sobrerol was later prepared from (±)-*cis*-carveol.

Dehydration of *trans*-sobrerol, first observed by Sobrero (*Compt. rend.*, 1851, **33**, 67) and later studied by Armstrong and Pope (*J.*, 1891, **59**, 315) and by Wallach (*Annalen*, 1893, **277**, 133), has been found to give pinol. We have found, however, that when the diol was acetylated and distilled at atmospheric pressure, acetic acid was split off and (±)-*trans*-carveol was obtained, the hydration being simply reversed.

Another autoxidation product of limonene, (+)-*cis*-*p*-menth-8-ene-1 : 2-diol, recently described in detail by Schmidt (*Chem. Ber.*, 1949, **82**, 11), when acetylated and subjected to thermal decomposition yields a mixture of carveols, amongst which (±)-*trans*-carveol has been identified (phenylurethane and hydrogen phthalate) in a preparation with a low positive rotation. This confirms Simonsen and Owen's suggestion ("The Terpenes," 2nd edn., 1947, Vol. 1, p. 154) that *cis*-*p*-menth-8-ene-1 : 2-diol is the primary oxidation product of limonene in moist air.

In this preparation (±)-*trans*-carveol is accompanied by a product which seems to be a hitherto unknown carveol in which a CH_2 group is attached to $C_{(1)}$ and is isomerised by acid to the Δ^1-compound. This is indicated by the difference in odour from *trans*-carveol, the odour of which is somewhat similar to that of crude naphthalene, and by the fact that

it is not racemised so readily with cold acid. Furthermore, it did not give a crystalline phenylurethane and on oxidation afforded, in poor yield, an optically active ketone, which gave a semicarbazone with a very wide melting range. Hydrolysis of the semicarbazone gave an odour reminiscent of cuminaldehyde and quite different from that of carvone.

Considerable dehydration of this new carveol took place during the thermal decomposition, and the optically active hydrocarbon formed is probably another terpene of formula $C_{10}H_{14}$ (cf. Wallach's hydrocarbon, *Annalen*, 1891, **264**, 27; verbenene, *Ber.*, 1921, **54**, 887; and camphenene, *Ber.*, 1928, **61**, 1491).

Schmidt (*loc. cit.*) also describes (+)-*trans*-*p*-menth-8-ene-1 : 2-diol, first prepared by Ginzberg from (+)-*p*-menthane-1 : 2 : 8-triol, an oxidation product of (+)-α-terpineol (*Ber.*, 1896, **29**, 1198). Acetylation of this triol, without isolation of the diol, has now been found to yield (±)-*cis*-carveol by thermal decomposition.

On hydration, (±)-*cis*-carveol yielded a sobrerol; as the m. p. 107—108° was much lower than that of (±)-*trans*-sobrerol, we consider it to be the *cis-form*. When heated with dilute sulphuric acid it formed pinol. After (±)-*cis*-sobrerol had been kept for 2 years its melting point had changed into that of the *trans-form*.

Experimental

Light petroleum refers to the fraction of b. p. 40—60°. All optical rotations are measured in 1-dm. tubes.

(−)-Carvone [isolated from oil of spearmint; α_D^{20} −57·8° (homogeneous)] was reduced by Ponndorf's method as described by Macbeth and Mills (*J.*, 1949, 2646). The mixture of *cis*- and *trans*-carveol obtained had α_D^{20} −122·1° (homogeneous).

Racemisation.—A solution of sulphuric acid (1 g.) in dry ether (9 g.) was cooled to 2° and slowly added to the above carveol mixture (2 g.) in dry ether (8 g.), also at 2°, and the whole kept at 6°; the optical rotation was −4·9° after 2½ hours and only −0·8° after 24 hours. A corresponding 10% solution in dry ether had α_D −7·3° initially and this was unchanged after 24 hours.

(±)-trans-*Carveol.*—(*a*) The carveol mixture (α_D −122·1°; 55 g.) was heated with phthalic anhydride (50 g.) and pyridine (2·5 g.) for 6 hours at 120°. The only crystalline product obtained was a hydrogen phthalate, m. p. 136—137° (9·5 g.), which on hydrolysis gave (±)-*trans*-carveol, b. p. 95—100°/5 mm., d_4^{18} 0·950, n_D^{20} 1·4956, α_D ±0°. This formed a phenylurethane, m. p. 94—95°, identical (m. p. and mixed m. p.) with that of carveol from autoxidised limonene. This was identified by its 3 : 5-dinitrobenzoate, m. p. 119° (Johnston and Read, *loc. cit.*).

(*b*) (±)-*trans*-Sobrerol (2·5 g.) and acetic anhydride (5 g.) were refluxed for 5 hours and slowly distilled at 80 mm. pressure. Two fractions were obtained: (i) b. p. 71°, (ii) b. p. up to 178°. The latter was distilled at atmospheric pressure, and the distillate washed till neutral and hydrolysed with excess of alcoholic sodium hydroxide. After steam-distillation, extraction with light petroleum, and drying at 100°/80 mm., it had d_4^{23} 0·950, n_D^{20} 1·4949, α_D ±0°, and had the typical unpleasant odour of *trans*-carveol. It formed a phenylurethane, m. p. 94—95°, undepressed by authentic (±)-*trans*-carveol phenylurethane.

(±)-trans-*Sobrerol.*—Carveol mixture (α_D −122·1°; 12 g.) was shaken with a solution of benzenesulphonic acid (30 g.) in 5% sulphuric acid (1200 c.c.) at room temperature for 24 hours. The solution was extracted with light petroleum (50 c.c.), the solvent removed *in vacuo*, and the residue distilled, forming fractions: (i) b. p. <73°/100 mm. (2 g.), and (ii) b. p. 80—135°/100 mm., α_D −14·1° (homogeneous), mostly carveol but containing 10·1% of ketones estimated as carvone (3 g.), and a residue (0·5 g.). The last crystallised on cooling and formed shiny scales, m. p. 119—121°, from light petroleum. It is insoluble in water.

Fraction (i) contained pinol, which formed the dibromide, m. p. 94—95°, on treatment with bromine in carbon tetrachloride, evaporation *in vacuo*, and crystallisation from light petroleum.

The acid aqueous solution was made alkaline with sodium carbonate and twice extracted with ethyl acetate. On evaporation, the extracts left a waxy residue of (±)-*trans*-sobrerol which, crystallised from ethyl acetate, had m. p. 131—131·5°, α_D ±0°. This was identical (m. p. and mixed m. p.)with an authentic sample from Americal oil of turpentine.

Thermal Decomposition of Acetylated (+)-cis-p-*Menth*-8-*ene*-1 : 2-*diol.* This diol (m. p. 72·5—73·5°; prepared from orange-oil terpenes; 67 g.) and acetic anhydride (70 g.) were refluxed for 8 hours, and the mixture then distilled very slowly at atmospheric pressure, yielding

fractions b. p. <133° (mainly acetic acid), b. p. 133—150° (α_D +37·9°), and b. p. 150—210°. The last two fractions were washed till neutral, and the oil (35 g.) refluxed with excess of sodium hydroxide in alcohol for 2 hours. After distillation in steam and separation, there were obtained two fractions: (i) α_D +37·7°, (ii) α_D +40·2°. Fraction (i) was fractionated *in vacuo*, giving fractions (*a*) b. p. 46—56°/3 mm., 172—174° 766 mm., d_4^{20} 0·8802, n_D^{20} 1·4982, α_D +41·9° (6 g.), and (*b*) b. p. 56—83°/3 mm., α_D +32·3° (3·5 g.); (*a*) is obviously a hydrocarbon but no crystalline bromide or nitrosite could be prepared from it. After about 3 months it had polymerised to an amorphous, brittle substance melting indefinitely about 68—70°.

Redistillation of the higher-boiling fractions (ii) and (i) (*b*) gave a rather viscous end-fraction, b. p. 93°/3 mm., α_D +52·2°, d_4^{20} 0·956, n_D^{20} 1·4967. It did not form a crystalline phenylurethane, but considerable diphenylurea was formed; a 3 : 5-dinitrobenzoate, however, m. p. 80—80·5°, was obtained. The optical rotation of this carveol was unaffected by sulphuric acid in ether at 6° but fell from 52·2° to 51·1° when the product itself was kept for 3 months in a closed vessel.

In a second experiment, the carveol fraction had α_D +14° and yielded (±)-*trans*-carveol phenylurethane, m. p. 94—95°, and (±)-*trans*-carveyl hydrogen phthalate, m. p. 136—137°, although only in small quantities. The hydrocarbon fraction, purified by fractionation and by repeated washing with 70% alcohol, had α_D +47·6°, d_4^{17} 0·878, n_D^{17} 1·4956.

In a third experiment the carveol fraction had α_D +35·4°. When it (9·5 g.) was oxidised in 50% acetic acid solution (10 g.) with chromium trioxide (9 g.) in 75% acetic acid at 0°, the ketone obtained on steam-distillation (1·75 g.) had α_D +37·4°. The m. p. of its semicarbazone (softening at 155°, m. p. 175—180°) indicated that it was not uniform and heating with aqueous phthalic acid produced an odour resembling that of cuminaldehyde, quite different from that of carvone.

(±)-cis-*Carveol.*—(±)-*p*-Menthane-1 : 2 : 8-triol [86 g.; m. p. 122—124°, prepared by oxidation of (±)-α-terpineol] and acetic anhydride (150 g.) were refluxed for 8 hours. After slow distillation at atmospheric pressure and washing with brine, an oil (79 g.) was obtained; this was hydrolysed with excess of sodium hydroxide in alcohol, and steam-distillation then removed a volatile oil, leaving a substantial residue of diol and triol. The volatile oil on distillation gave: (i) b. p. <84°/3 mm., $n_D^{23\cdot5}$ 1·5004 (3 g.); (ii) b. p. 84—87°/3 mm., $d_4^{23\cdot5}$ 0·9497, $n_D^{23\cdot5}$ 1·4978, (9 g.); (iii) b. p. 90—92°/3 mm., $n_D^{23\cdot5}$ 1·4988 (2·5 g.); (iv) b. p. mainly 103—108°/3 mm., $n_D^{23\cdot5}$ 1·4939 (5 g.).

Fraction (i) with phthalic anhydride (2 g.) gave (±)-*cis*-carveyl hydrogen phthalate, which formed needles, m. p. 114—116°, from light petroleum. The corresponding *trans*-ester is hardly soluble in this solvent. On refractionation of (ii), the main product had b. p. 92—94°/3 mm., d_4^{25} 0·954, n_D^{25} 1·4970, and when oxidised with chromium trioxide as described above yielded a steam-volatile ketone, which formed a semicarbazone, m. p. 154—156°, after recrystallisation. This was identical (m. p. and mixed m. p.) with an authentic specimen of (±)-carvone semicarbazone.

(±)-*cis*-Carveol does not form a crystalline phenylurethane.

(±)-cis-*Sobrerol.*—(±)-*cis*-Carveol (4 g.) was shaken with dilute sulphuric acid (5%, 400 g.) for 24 hours at room temperature. Unchanged oil (2 g.) was separated and re-treated, and the solutions were combined, washed twice with light petroleum, made alkaline with sodium carbonate, and concentrated *in vacuo*. By exhaustive extraction with ethyl acetate (±)-cis-*sobrerol* was obtained as a viscous oil, which crystallised in the presence of a drop of water. It formed short, sparkling prisms, m. p. 107—108°, from water (Found: C, 70·8; H, 10·6. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%). Mixed with (±)-*trans*-sobrerol, it melted from 92° to 110°. A pure sample after 2 years had m. p. 131—131·5°, undepressed by authentic (±)-*trans*-sobrerol.

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849. *Fluoro-olefins. Part I. The Synthesis of Hexafluorobuta-1 : 3-diene.*

By R. N. Haszeldine.

A general method for the synthesis of fluorohalogenobutadienes * is described and illustrated by the conversion of chlorotrifluoroethylene into hexafluorobuta-1 : 3-diene in 80% yield. Addition of iodine monochloride or monobromide to chlorotrifluoroethylene gives chlorofluoro- and bromochlorofluoroiodo-compounds, which react readily with mercury in ultra-violet light or with zinc in dioxan, to yield hexafluoro-1 : 2 : 3 : 4-tetrahalogenobutanes. Dehalogenation of the last compounds with zinc and ethanol affords hexafluorobutadiene. Syntheses of certain fluoro- and fluorohalogeno-butenes, including octafluorobut-2-ene, are described, and infra-red and ultra-violet spectra are presented and discussed.

Tetrafluoroethylene is of great value in synthetic organic fluorine chemistry and is finding industrial application. Potentially as important is hexafluorobuta-1 : 3-diene, but the only synthesis for this compound yet described is that by Miller *et al.* (*Ind. Eng. Chem.*, 1947, **39**, 401). Direct fluorination of 1 : 2-dichlorodifluoroethylene at −78° gave a fluorine-containing dimer $C_4Cl_4F_6$, in 44% optimum yield, as well as the expected dichlorotetrafluoroethane; dechlorination of the compound $C_4Cl_4F_6$ afforded hexafluorobutadiene. The disadvantages of this method are that elementary fluorine is required, the yield of $C_4Cl_4F_6$ is low, and by-products such as chloropentafluoroethane, 1 : 1 : 2-trichlorotrifluoroethane, 1 : 2-difluorotetrachloroethane, a pentachloropentafluorobutane, and a hexachlorotetrafluorobutane, are produced. Using hexafluorobutadiene prepared in this way, Miller and his co-workers (*loc. cit.*; Prober and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 598) have shown the potential interest of hexafluorobutadiene and have reported its polymerisation initiated by heat or by fluorine. Since the work reported below was completed, Miller ("Preparation and Properties and Technology of Fluorine and Organic Fluoro-compounds," Editors Glasser and Schram, McGraw Hill, 1951, pp. 567—685) has reported an alternative procedure developed during the recent war for the preparation of hexafluorobutadiene from chlorotrifluoroethylene involving pyrolysis at 500°, to give 3 : 4-dichlorohexafluorobut-1-ene, followed by dechlorination. The yields by this procedure are apparently low (30—40%).

A simple general method for the conversion of suitable fluoroethylenes into dienes is now illustrated by the preparation of hexafluorobutadiene from commercially available chlorotrifluoroethylene.

Addition of iodine monochloride or monobromide to chlorotrifluoroethylene gives 1 : 2-dichloro- (I) and 1-bromo-2-chloro-1 : 1 : 2-trifluoroiodoethane (II) in almost quanti-

$CClF_2{\cdot}CClIF$	$CBrF_2{\cdot}CClIF$	$ClF_2{\cdot}CCl_2F$	$CClF_2{\cdot}CHClF$
(I)	(II)	(III)	(IV)

tative yield. The reaction takes place readily under slight pressure in absence of a solvent, or somewhat more slowly when the chlorotrifluoroethylene is passed through a suspension of the iodine halide in solvents such as carbon tetrachloride, 1 : 1 : 2-trichlorotrifluoroethane, 1 : 2-dibromo-1-chlorotrifluoroethane, or any fluoro- or fluorohalogeno-compound of suitable boiling point. The use of (I) or (II) as reaction media is also convenient, since the necessity for subsequent efficient fractional distillation is thereby removed. As might be expected the addition of iodine chloride occurs at a much lower temperature than that of iodine bromide. The only by-product is the compound in which the iodine atom in (I) or (II) has been replaced by chlorine or bromine. This is ascribed either to the reaction of chlorotrifluoroethylene with chlorine or bromine (formed by dissociation of the iodine halide into iodine and halogen), or to the secondary reaction of (I) or (II) with the iodine halide or halogen. The by-products 1 : 1 : 2-trichlorotrifluoroethane and 1 : 2-dibromo-1-chlorotrifluoroethane are dehalogenated to chlorotrifluoroethylene in almost theoretical yield, so that the preparation of (I) and (II) is essentially quantitative.

* Used in this sense, "halogen" excludes fluorine.

The constitution of (I) follows from its conversion into the known 1 : 2-dichlorotetrafluoroethane and thence into tetrafluoroethylene [(I) $\longrightarrow$ $(CClF_2)_2$ $\longrightarrow$ C_2F_4; cf. the possible isomer (III) which would yield 1 : 1-dichlorotetrafluoroethane], by mild treatment with cobalt trifluoride. It is confirmed by conversion of (I) into (IV) by irradiation in a solvent from which hydrogen is readily abstracted by the fluorohalogeno-radical:

$$(I) \xrightarrow[Hg]{Light} CClF_2{\cdot}CClF{\cdot} \xrightarrow{RH} (IV) \qquad (+ R{\cdot})$$

Zinc and ethanol removed chlorine from (IV), to give the known trifluoroethylene [cf. (III) which would yield 1 : 1-dichloro-1 : 2 : 2-trifluoroethane; this compound is probably inert to zinc under the conditions used, but if anything would give 1-chloro-1 : 2-difluoroethylene]. Barr, Gibson, and Lafferty (*ibid.*, 1951, **73**, 1352) have recently described the preparation of (I), but assigned the structure only by analogy.

The structure of (II) was proved in a similar manner. Reaction with cobalt trifluoride gave 1-bromo-2-chlorotetrafluoroethane, and thence tetrafluoroethylene by removal of equimolar amounts of bromine and chlorine. The possible isomer (V) would have given 1-bromo-1-chlorotetrafluoroethane. Irradiation of (II) in a hydrogen-containing organic

$$(V) \quad ClF_2{\cdot}CClBrF \qquad\qquad CBrF_2{\cdot}CHClF \quad (VI)$$

solvent gave (VI), which was converted into trifluoroethylene by removal of equimolar amounts of bromine and chlorine [(V) would have given 1-bromo-1-chloro-1 : 2 : 2-trifluoroethane].

The direction of addition of I^+X^- to chlorotrifluoroethylene is in agreement with the addition of alcohols and amines under conditions favouring ionic reactions (Hanford and Rigby, U.S.P. 2,409,274/1946; Miller, Fager, and Griswold, *J. Amer. Chem. Soc.*, 1948, **70**, 431; Young and Tarrant, *ibid.*, 1949, **71**, 2432; Pruett *et al.*, *ibid.*, 1950, **72**, 3646). In all instances the negative substituent becomes attached to the $:CF_2$ group; this may be attributed to importance of resonance forms $\bar{F}\ \overset{+}{C}F{:}CClF \longleftrightarrow CF_2{:}\overset{+}{C}ClF \longleftrightarrow F{:}CF{\cdot}\bar{C}ClF$ giving a polarisation $\overset{\delta+}{C}F_2{:}\overset{\delta-}{C}ClF$.

Photochemical chlorination or bromination of (I) yielded 1 : 1 : 2-trichloro- and 1-bromo-1 : 2-dichloro-trifluoroethane, and of (II) yielded 1-bromo-2 : 2-dichloro- and 1 : 2-dibromo-1-chloro-trifluoroethane. (I) readily combines with mercury in ultraviolet light, to give 1 : 2-dichloro-1 : 2 : 2-trifluoroethylmercuric iodide. Irradiation under more stringent conditions gives the mercuric iodide only transiently, if at all, and the 1 : 2-dichloro-1 : 1 : 2-trifluoroethyl radical dimerises to give 1 : 2 : 3 : 4-tetrachlorobutane in high yield:

$$CClF_2{\cdot}CClF \xrightarrow[Light]{Hg,} (CClF_2{\cdot}CClF)_2 \qquad (VII)$$

The butane (VII) is also formed by photolysis of the mercuri-iodide in an inert solvent (perfluoromethyl*cyclo*hexane). Dimerisation of the bromo-compound (II) similarly yields 1 : 4-dibromo-2 : 3-dichlorohexafluorobutane. Thus the replacement of fluorine in the trifluoromethyl or pentafluoromethyl radicals (which dimerise with difficulty and are often preferentially decomposed on the glass or silica of the containing vessel) by chlorine or bromine gives radicals of decreased activity and longer life, which dimerise readily. Dehalogenation of the hexafluoro-1 : 2 : 3 : 4-tetrahalogenobutanes to hexafluorobuta-1 : 3-diene is almost quantitative.

Conversion of (I) into hexafluorobutadiene is more conveniently effected by the preferential coupling by intermolecular deiodination when a concentrated solution of (I) in dioxan is treated at low temperatures with zinc. Under such conditions the intramolecular dehalogenation of (I) to chlorotrifluoroethylene occurs to only a slight extent. By increasing the temperature, (VII) can then be converted *in situ* into hexafluorobutadiene.

The possibility of hexafluoro*cyclo*butene formation from (VII) by the sequence:

$$\begin{matrix} CClF_2{\cdot}CClF \\ CClF_2{\cdot}CClF \end{matrix} \xrightarrow[EtOH]{Zn-} \begin{matrix} CF_2{-}CF \\ | \quad\ | \\ CF_2{-}CF \end{matrix}$$

can be eliminated, since the products absorb two molecules of chlorine or bromine to give the hexafluoro-1 : 2 : 3 : 4-tetrahalogenobutanes. Furthermore, the presence of two conjugated double bonds in the diene, which readily decolorises acetone–permanganate, is shown by the ultra-violet and the infra-red spectrum. The considerably more powerful absorption of hexafluorobutadiene is apparent from the Table where it is compared with four mono-olefins containing only carbon and fluorine.

Extinction coefficients.

λ(mμ):	230	225	220	215	210	206
$CF_2{:}CF{\cdot}CF{:}CF_2$	250	430	760	1350	2130	2800
$CF_3{\cdot}CF{:}CF{\cdot}CF_3$	2·2	3·2	4·6	6·8	11·6	—
$CF_3{:}CF_2$	0·3	1·0	2·1	3·8	6·0	10·0
$CF_3{\cdot}CF{:}CF_2$	0·03	0·06	0·08	0·14	0·30	0·65
$\overbrace{CF_2{\cdot}CF{:}CF{\cdot}CF_2}$	—	0·02	0·04	0·08	0·13	0·18

The most significant point in the Table is that the intensity of absorption of hexafluorobutadiene is much less than that of butadiene ($\lambda_{max.}$ 217 mμ, ε = 21,000; Smakula, *Angew. Chem.*, 1934, **47** 657) or of hexachlorobutadiene ($\lambda_{max.}$ 251·5 mμ, ε = 4400; $\lambda_{max.}$ 222 mμ, ε = 17,800; $\lambda_{min.}$ 244·5 mμ, ε = 4200). Thus replacement of hydrogen by chlorine produces an extra band at longer wave-length, although there is still the "typical" butadiene band at 220 mμ with ε *ca.* 20,000, whereas on replacement of hydrogen by fluorine the butadiene band at 220 mμ is considerably displaced to a lower wave-length. This, and the reduction in intensity of absorption, indicate that the unsaturation electrons in hexafluorobutadiene are much more localised and are available for conjugation to a much smaller extent than might have been expected.

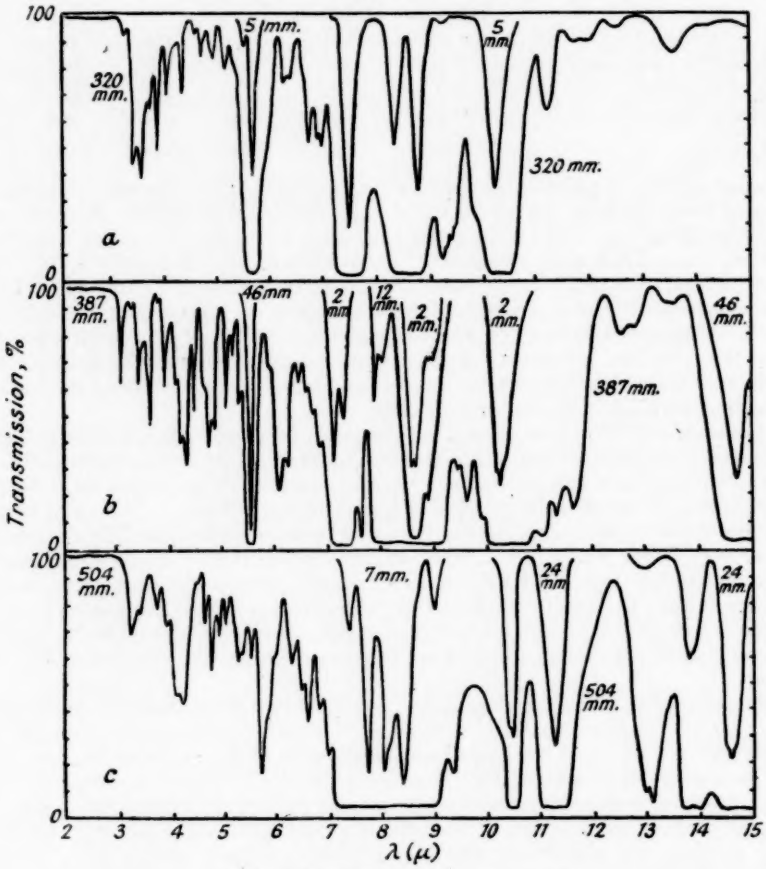
Butadiene shows C=C absorption in the infra-red at 6·24 and 6·30 μ (doublet), a marked shift to longer wave-length compared with ethylene (6·16 μ); the replacement of hydrogen by chlorine to give hexachlorobutadiene causes a further displacement to 6·39 μ. The C=C absorption in hexafluorobutadiene (Fig. 1*a*) is, for a diene, at the remarkably low wave-length of 5·65 μ, and comparison with that in tetrafluoroethylene (5·35 μ; Torkington and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 236) and with the C=C absorption at 5·56 μ in compounds of the type $R{\cdot}CF{:}CF_2$ (R = H, Cl, CF_3, or C_2F_5) (unpublished data; see below) reveals that the conjugation effect exists, but is small. The spectrum of hexafluorobutadiene is of great value for characterisation, and that of the isomeric hexafluoro-*cyclo*butene (Fig. 1*b*) is sufficiently different to render feasible its detection as impurity in the diene.

Octafluorobut-2-ene has been prepared from chlorotrifluoroethylene or hexafluorobutadiene *via* 1 : 4-dichlorohexafluorobut-2-ene. The last compound is obtained by partial dechlorination of 1 : 2 : 3 : 4-tetrachlorohexafluorobutane with zinc and dioxan; dehalogenation is slow at room temperature, and under vigorous reflux yields only hexafluorobutadiene, but with suitable intermediate conditions moderate yields of the dichloro-compound may be obtained. The 1 : 4-dichlorohexafluorobut-2-ene absorbs chlorine or bromine, to give the hexafluorotetrahalogenobutanes (which readily give hexafluorobutadiene with zinc and ethanol), and on oxidation yields chlorodifluoroacetic acid; treatment with zinc and ethanol or with zinc alone fails to give hexafluorobutadiene. The possible alternative products of the zinc–dioxan dehalogenation, 1 : 2-dichlorohexafluoro*cyclo*butane and 3 : 4-dichlorohexafluorobut-1-ene, can thus be eliminated. The chlorine atoms in 1 : 4-dichlorohexafluorobut-2-ene, like other allylic halogen atoms in the system $C{:}C{\cdot}CF_2X$, are much more reactive to bases, amines, ammonia, etc., than is the chlorine atom in, say, chloroheptafluoropropane. In particular, treatment under mild conditions with antimony trifluoride gives a high yield of octafluorobut-2-ene [$(CClF_2{\cdot}CClF)_2 \longrightarrow (CClF_2{\cdot}CF{:})_2 \longrightarrow (CF_3{\cdot}CF{:})_2$], the structure of which was proved by its reaction with chlorine and bromine and by its oxidation to 1·5 mols. of trifluoroacetic acid.

The boiling points of octafluoro-but-1-ene, -but-2-ene, and -*iso*butene are very similar, but these compounds are readily distinguished from each other and from others of similar boiling point (*e.g.*, perfluoro-*n*-butane, hexafluoro*cyclo*butene, hexafluorobutadiene) by their infra-red spectra. That of octafluorobut-2-ene is shown in Fig. 1*c* and, if the band

at 5·77 μ is attributed to the C=C stretching vibration, it follows that the but-2-ene contains at least some of the *cis*-isomer. This interpretation is supported by the band at 5·74 μ in perfluoro*cyclo*hexene where *cis*-configuration is essential; the low value of 5·59 μ for hexafluoro*cyclo*butene is attributed to ring strain. As might be expected from the fact that they contain three fluorine atoms attached to the double bond, the C=C stretching

FIG. 1*a*—*c*.



a, CF_2:CF·CF:CF_2, *vapour in* 50 *mm. cell.*
b, CF_2·CF:CF·CF_2, ,, 100 ,,
c, CF_3·CF:CF·CF_3, ,, 50 ,,

absorption in octafluorobut-1-ene and hexafluoropropene is at 5·56 μ, nearer to that of tetrafluoroethylene.

The addition of bromine or chlorine to hexafluorobutadiene under conditions favouring a free radical reaction proceeds stepwise. At room temperature one molecule of bromine is absorbed to give, quantitatively, a mixture (*A*) of 1 : 4-dibromehexafluorobut-2-ene and 3 : 4-dibromohexafluorobut-1-ene. Photochemical chlorination at low temperature similarly yields a mixture of 1 : 4-dichlorohexafluorobut-2-ene and 3 : 4-dichlorohexafluorobut-1-ene, but 1 : 2 : 3 : 4-tetrachlorohexafluorobutane and unchanged hexafluorobutadiene were also detected; the rates of addition of chlorine to hexafluorobutadiene and to one, or both, of the dichlorohexafluorobutenes are clearly comparable. The hexafluoro-1 : 4- and

-3 : 4-dihalogenobutenes are easily distinguished by infra-red spectroscopy. In the following Table are given the C=C stretching vibrations of olefins containing the $\cdot CF{:}CF_2$

	$CF_2{:}CClF$	$CF_2{:}CHF$	$CF_2{:}CF\cdot CF_3$	$CF_2{:}CF\cdot C_2F_5$	$(CF_2{:}CF)_2$	$(CF_2\cdot CF{:})_2$
λ (μ)	5·57	5·57	5·56	5·56	5·65	5·77

or $\cdot CF{:}CF\cdot$ groups. It is evident that compounds containing a double bond of the first type have a band at *ca.* 5·56 μ, whereas those with a double bond of the second type have a band at *ca.* 5·77 μ. Considering now the compound $CXF_2\cdot CXF\cdot CF{:}CF_2$, it can be predicted that it will show a band in the C=C stretching region at *ca.* 5·60 μ, the increase in wave-length being due to replacement of the C_2F_5 group by the heavier and less electronegative $CClF_2\cdot CClF$ group. Similarly, the C=C stretching vibration in $(CXF_2\cdot CF{:})_2$ would be predicted at *ca.* 5·80 μ. The mixture of the dibromo-compounds shows bands at 5·62 and 5·85 μ, and of the dichloro-compounds show bands at 5·61 and 5·84 μ.

Treatment of the mixture (*A*) (X = Br) with zinc and ethanol converted the 3 : 4-dibromo-compound present into hexafluorobutadiene. The unchanged material then showed only one band in the C=C stretching region, at 5·85 μ, and was the 1 : 4-dibromo-compound; treatment with antimony trifluorodichloride converted it into octafluorobut-2-ene. The ratio of 3 : 4- to 1 : 4-addition products was approximately 2 : 3. Reversal of the procedure, *i.e.*, treatment of the mixture of dibromohexafluorobutenes first with antimony trifluorodichloride, then with zinc and ethanol, gave a ratio of 1 : 1, so that isomerisation may take place during reaction :

$$Br\cdot + C_4F_6 \longrightarrow CBr_2F\cdot\dot{C}F\cdot CF{:}CF_2 \xrightarrow{Br_2} CBrF_2\cdot\dot{C}BrF\cdot CF{:}CF_2$$

$$\updownarrow \qquad\qquad (Zn\text{–}EtOH)\downarrow\uparrow(SbF_3Cl_3)$$

$$CBrF_2\cdot CF{:}CF\cdot CF_2\cdot \xrightarrow{Br_2} CBrF_2\cdot CF{:}CF\cdot CBrF_2$$

Application of the dehalogenation technique to the mixture of dichlorohexafluorobutenes similarly removed the 3 : 4-dichloro-compound, and the residual dichloro-compound (C=C stretching vibration 5·84 μ) was easily converted into octafluorobut-2-ene; the ratio of hexafluoro-3 : 4- to -1 : 4-dihalogenobutenes was 1 : 2. Some 1 : 2 : 3 : 4-tetrachlorohexafluorobutane was formed during the initial reaction with chlorine, however, so this ratio may be nearer to 3 : 4, since it is to be expected that a compound $CXF_2\cdot CXF\cdot CF{:}CF_2$ will be more susceptible to radical attack than will $(CXF_2\cdot CF{:})_2$.

Experimental

Addition of Iodine Monochloride to Chlorotrifluoroethylene.—Chlorotrifluoroethylene (11·65 g., 0·10 mole) was condensed into an evacuated steel bomb (capacity 300 ml.), fitted with a needle valve and pressure gauge and containing iodine monochloride (20 g., 0·12 mole). The bomb was sealed and warmed to 35—40° to melt the iodine monochloride. An exothermic reaction set in on shaking, and the pressure reached a maximum of 9 atm. before dropping rapidly to 1 atm. The initial reaction was complete after 10 minutes, and after 2 hours the contents of the bomb were removed by pumping through a trap cooled in liquid air. All the chlorotrifluoroethylene had been converted into a liquid product which, after treatment with sodium thiosulphate to remove traces of iodine, was dried (P_2O_5) and distilled, giving 1 : 1 : 2-trichlorotrifluoroethane (1%), b. p. 47·5—48·0°, n_D^{25} 1·355 (Locke, Brode, and Henne, *J. Amer. Chem. Soc.*, 1934, **56**, 1726, report b. p. 47·6, n_D^{25} 1·3557), and 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (27·1 g., 97%), b. p. 99—99·5°, n_D^{20} 1·449, a colourless liquid becoming pink on exposure to light (Found : C, 8·7; I + Cl, 70·9%; *M*, 275, 280. Calc. for $C_2Cl_2IF_3$: C, 8·6; I + Cl, 71·0%; *M*, 279). Ultra-violet absorption spectrum in ethanol : Max., 261 mμ, ε = 295; Min. 233 mμ, ε = 190. Barr *et al.* (*loc. cit.*) reported b. p. 43—44°/100 mm., n_D^{25} 1·4474, for the compound obtained by the interaction of iodine chloride and chlorotrifluoroethylene.

On a larger scale, the bomb containing iodine monochloride (54 g., 0·33 mole) was evacuated, heated to 30°, and connected by a flexbile-metal pressure-tube to a cylinder of chlorotrifluoroethylene. The olefin was slowly admitted to the continuously shaken bomb, at such a rate that the temperature did not rise above 40°, until no more was absorbed (2 hours). The excess of chlorotrifluoroethylene was removed, and the residue on distillation gave 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (89·2 g., 96%). A small amount of iodine was left in the bomb.

In a reaction at atmospheric pressure, chlorotrifluoroethylene was passed by means of dispersion disc into a stirred suspension of iodine monochloride (16·2 g., 0·10 mole) in 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (80 ml.) at 45—50°. The unchanged olefin was recycled, and after 4 hours no further absorption occurred. After removal of iodine with sodium thiosulphate, the yield of distilled 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane was 87%, and of 1 : 1 : 2-trichlorotrifluoroethane 6%.

The 1 : 1 : 2-trichlorotrifluoroethane formed as a by-product was reconverted into chlorotrifluoroethylene in 95% yield by treatment with zinc and ethanol.

Proof of Structure of 1 : 2-*Dichloro*-1 : 2 : 2-*trifluoroiodoethane.*—(*a*) The iodo-compound (4·0 g.) was added dropwise during 1 hour to cobalt trifluoride (50 g.) in a horizontal copper reaction vessel at 190°. The volatile products were washed with water and fractionated *in vacuo*, to give chloropentafluoroethane (7%), b. p. −37° (Found: C, 15·3%; *M*, 155. Calc. for C_2ClF_5: C, 15·5%; *M*, 154·5) (Calfee, Fukuhara, Young, and Bigelow, *J. Amer. Chem. Soc.*, 1940, **62**, 267, report b. p. −38°), and 1 : 2-dichlorotetrafluoroethane (72%), b. p. 4° (Found: *M*, 170. Calc. for $C_2Cl_2F_4$: *M*, 171) (Locke, Brode, and Henne, *loc. cit.*, report b. p. 3·5°), shown to be free from isomers by its infra-red spectrum and by treatment with zinc and ethanol at 90° in a sealed tube to give tetrafluoroethylene (96%) identified by infra-red spectroscopy.

(*b*) Irradiation for 7 days of an ethanolic solution (10 ml.) of pyrogallol (0·3 g.) and 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (6·1 g.) shaken vigorously at 120° in a silica tube containing mercury (10 ml.) gave, on distillation, 1 : 2-dichloro-1 : 2 : 2-trifluoroethane (47%), b. p. 28·5° (Found: *M*, 152. Calc. for $C_2HCl_2F_3$: *M*, 153) (Henne and Ladd, *ibid.*, 1936, **58**, 402, report b. p. 28°). When this was heated with zinc and ethanol to 80° (sealed tube), chlorine (96%), and no fluorine, was removed to give trifluoroethylene, identified by infra-red spectroscopy.

Photochemical Chlorination and Bromination of 1 : 2-*Dichloro*-1 : 2 : 2-*trifluoroiodoethane.*—When exposed to ultra-violet radiation for 3 days, the iodo-compound (2·1 g.) and excess of chlorine in a silica vessel gave 1 : 1 : 2-trichlorotrifluoroethane (77%), b. p. 47—48° (Found: *M*, 186. Calc. for $C_2Cl_3F_3$: *M*, 187·5). Similar treatment of 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane with bromine yielded 1-*bromo*-1 : 2-*dichlorotrifluoroethane* (80%), b. p. 71·5—72·0° (Found: C, 10·1; Br + Cl, 65·1%; *M*, 231. $C_2Cl_2BrF_3$ requires C, 10·3; Br + Cl, 65·1%; *M*, 232).

Interaction of 1 : 2-*Dichloro*-1 : 2 : 2-*trifluoroiodoethane and Mercury.*—Mercury (10 ml.) and 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (12·0 g.) were sealed in an evacuated 100-ml. silica tube which was then shaken horizontally (vibro-shaker). Intimate mixing of the mercury and iodo-compound was thereby obtained, and on exposure to ultra-violet light from a Hanovia arc situated 5 cm. from the reaction vessel, mercuric iodide was rapidly deposited. Use of an excess of mercury prevents coating of the walls of the vessel by mercuric iodide. After 48 hours the liquid mixture was transferred by heating and pumping to a cooled trap, then distilled to give unchanged 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (5%), b. p. 99—100°, 1 : 2 : 3 : 4-*tetrachlorohexafluorobutane* (82%, calc. on iodo-compound), b. p. 134·0—134·5°, 75°/106 mm., n_D^{23} 1·382 (Found: C, 15·6; Cl, 46·4. $C_4Cl_4F_6$ requires C, 15·8; Cl, 46·7%), and an unidentified by-product (*ca.* 7%), b. p. *ca.* 95°/30 mm., n_D^{23} 1·394. Miller *et al.* (*Ind. Eng. Chem.*, 1947, **39**, 401) refer to 1 : 2 : 3 : 4-tetrachlorohexafluorobutane but record no physical data.

A similar experiment, carried out in a silica tube which was rocked gently during reaction, gave an 85% yield of 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (89%, calc. on the iodo-compound used) after 48 hours.

With the tube stationary during irradiation, the mercury–organic liquid interface became covered with mercuric iodide and, after 48 hours, the liquid reaction products consisted of 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (71%) and unchanged 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (5%). The ethereal extract of the solid products yielded, after removal of the ether and sublimation of the residual solid, 1 : 2-*dichloro*-1 : 2 : 2-*trifluoroethylmercuric iodide* (12%) (Found: C, 5·2; I, 26·0. $C_2Cl_2IF_3Hg$ requires C, 5·0; I, 26·5%), white plates recrystallised from chloroform to m. p. 92—94° and with an odour similar to that of trifluoromethylmercuric iodide (Emeléus and Haszeldine, *J.*, 1949, 2948). On exposure to ultra-violet light while suspended in perfluoromethyl*cyclo*hexane, the mercurial (2·3 g.) was converted into mercuric iodide and 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (61%).

Preparation of Hexafluorobutadiene.—To a well-stirred suspension of zinc dust (100 g.) in ethanol (100 ml.) heated under an efficient water condenser leading to traps cooled in liquid air, was added dropwise during 5 hours 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (30·4 g., 0·1 mole) in ethanol (10 ml.). Steady gas evolution took place, and after a further 2 hours the contents of the liquid-air traps were passed through 5% sodium hydroxide and distilled *in vacuo*, to

give hexafluorobutadiene (15·7 g., 98%), b. p. 5·8° (Found: C, 29·5; F, 70·2%; *M*, 162. Calc. for C_4F_6: C, 29·6; F, 70·4%; *M*, 162). Prober and Miller (*loc. cit.*) report b. p. 6·5—7·5°.

For comparison of infra-red spectra, hexafluoro*cyclo*butene, b. p. 1·2°, was synthesised by cyclisation of chlorotrifluoroethylene at 200° in an autoclave, followed by dechlorination of the 1 : 2-dichlorohexafluoro*cyclo*butane with zinc and boiling ethanol. Harmon, U.S.P. 2,433,844/1948, reports b. p. 1·1°.

Conversion of 1 : 2-*Dichloro*-1 : 2 : 2-*trifluoroiodoethane into Hexafluorobutadiene.*—To a vigorously stirred suspension of zinc (30 g.) in dioxan (35 ml.) at 25—30° was slowly added 25% of a solution of 1 : 2-dichloro-1 : 2 : 2-trifluoroiodoethane (17·0 g.) in dioxan (10 ml.). After a further 20 minutes, the temperature was slowly raised to 50° (or to 100° to produce hexafluorobutadiene), and, after cooling to 25° again, a second 25% of the iodo-compound solution was slowly added. This cycle of operations was repeated until complete addition of the chlorofluoroiodide had been achieved. The volatile products at this stage were chlorotrifluoroethylene (40%) and a trace of hexafluorobutadiene. Care must be taken with the intermolecular deiodination carried out in this way. If the temperature is too low, or the solution of iodo-compound too dilute, little deiodination occurs initially and when the temperature is raised a very vigorous reaction sets in which leads to almost complete chlorotrifluoroethylene formation. If the temperature is too high, intramolecular dehalogenation occurs to the exclusion of intermolecular deiodination. The intramolecular dehalogenation is favoured in ethanolic solution, and the use of dioxan, benzene, or a higher alcohol is advantageous for coupling.

The 1 : 2 : 3 : 4-tetrachlorohexafluorobutane formed by the intermolecular deiodination is converted into hexafluorobutadiene *in situ* under reflux. The total yield of hexafluorobutadiene, separated from chlorotrifluoroethylene in a vacuum system, is 60%.

Synthesis of Octafluorobut-2-ene.—1 : 2 : 3 : 4-Tetrachlorohexafluorobutane (6·10 g.) was treated with zinc powder (20 g.) and anhydrous dioxan (50 ml.) at 55—70° under a reflux condenser at such a temperature that the required product distilled off as soon as formed. After 2 hours the distillate was shaken with water; the gaseous product was hexafluorobutadiene (15%), and removal and distillation of the lower layer from the aqueous medium gave 1 : 4-*dichlorohexafluorobut-2-ene* (2·46 g., 40%), b. p. 65·0—65·5°, n_D^{25} 1·339 (Found: C, 20·7; Cl, 30·4%; *M*, 232. $C_4Cl_2F_6$ requires C, 20·6; Cl, 30·5%; *M*, 233), shown by infra-red spectroscopy to be free from 3 : 4-dichlorohexafluorobut-1-ene. The dioxan solution was filtered, excess of water was added, and the lower layer separated, dried, and distilled, to give unchanged 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (35%), which did not react with zinc and dioxan at room temperature during 48 hours. When the chloro-compound was added during 10 hours to zinc and refluxing dioxan, 95% of hexafluorobutadiene was formed.

With alkaline potassium permanganate (*J.*, 1950, 2789), 1 : 4-dichlorohexafluorobut-2-ene (2·1 g.) gave chlorodifluoroacetic acid (1·3 mols.), b. p. 122°, characterised as its amide (Swarts, *Bull. Acad. roy. Belg.*, 1906, **50**, 42; 1907, **52**, 339).

Dropwise addition of 1 : 4-dichlorohexafluorobut-2-ene (2·3 g.) in ethanol (5 ml.) to zinc powder (10 g.) and refluxing ethanol (20 ml.) failed to yield hexafluorobuta-1 : 3-diene after 3 hours. Traces of a compound believed to be 1 : 1 : 2 : 3 : 4 : 4-hexafluorobut-2-ene were formed by reduction.

On reaction in ultra-violet light with a slight excess of chlorine, 1 : 4-dichlorohexafluorobut-2-ene (1·7 g.) gave a quantitative yield of 1 : 2 : 3 : 4-tetrachlorohexafluorobutane, identical with the compound described earlier. An excess of bromine similarly yielded 2 : 3-*dibromo*-1 : 4-*dichlorohexafluorobutane* (95%), b. p. 172—173°/760 mm., 78°/21 mm., n_D^{25} 1·425 (Found: C, 12·4; Br + Cl, 58·9. $C_4Br_2Cl_2F_6$ requires C, 12·2; Br + Cl, 58·8%), which on treatment with zinc and refluxing ethanol gave 95% of hexafluorobutadiene.

Antimony trifluoride (18 g.) and chlorine (0·5 g.) were sealed in a Carius tube, shaken vigorously, and heated gently until a homogeneous mass was obtained. The tube was opened and resealed with 1 : 4-dichlorohexafluorobut-2-ene (3·1 g.) condensed in from a vacuum system. Reaction was apparent at room temperature and was completed by 30 minutes' shaking and heating at 40°. The gaseous reaction product was octafluorobut-2-ene (2·26 g., 85%), b. p. 0·9° (Found: C, 24·0%; *M*, 199. Calc. for C_4F_8: C, 24·0%; *M*, 200). Henne and Newby (*J. Amer. Chem. Soc.*, 1948, **70**, 130) report b. p. 0·4—3·0°. With alkaline potassium permanganate this gave trifluoroacetic acid (1·5 mols.) identified as its amide. Octafluorobut-2-ene reacts quantitatively with chlorine or bromine on exposure to ultra-violet light, to give the dichloride, b. p. 63—64°, n_D^{25} 1·308 (Henne and Newby, *loc. cit.*, report b. p. 62·9°), and the *dibromide*, b. p. 96°, n_D^{25} 1·357 (Found: Br, 44·2. $C_4Br_2F_8$ requires Br, 44·4%). Minnesota Mining and Manufacturing Co. find b. p. 93° (personal communication).

Interaction of Iodine Bromide and Chlorotrifluoroethylene.—Chlorotrifluoroethylene (11·65 g.) and iodine monobromide (23 g.) in a steel bomb (capacity, 300 ml.) were heated from 30° to 100° during 2 hours. Preliminary experiments had shown that there was incomplete reaction at 60° for a similar period, but that reaction was essentially complete at 80° in 6 hours. Distillation gave unchanged chlorotrifluoroethylene (2%), 1 : 2-dibromo-1-chlorotrifluoroethane (4%), b. p. 92—92·5°, n_D^{25} 1·425 (Found: C, 8·6. Calc. for $C_2Br_2ClF_3$: C, 8·7%) (Locke, Brode, and Henne, *loc. cit.*, report b. p. 92·9°, n_D^{25} 1·4272), and 1-*bromo*-2-*chloro*-1 : 1 : 2-*trifluoroiodoethane* (84%), b. p. 82°/195 mm., n_D^{25} 1·482 (Found: C, 7·5; F, 17·4. $C_2ClBrIF_3$ requires C, 7·4; F, 17·6%). The last compound is partly decomposed by distillation at atmospheric pressure but can be distilled in the dark under partial vacuum as a colourless liquid which readily liberates iodine on exposure to light. Absorption spectrum in ethanol: Max. 267 mμ, ε = 370; Min. 241 mμ, ε = 280.

The structure of the bromo-iodo-compound was proved as follows. (*a*) Passage, during 4 hours, of 1-bromo-2-chloro-1 : 1 : 2-trifluoroiodoethane (4·9 g.) over cobalt trifluoride (50 g.) at 200° gave, after washing with water and distillation *in vacuo*, chloropentafluoroethane (12%) (Found: *M*, 156. Calc. for C_2ClF_5: *M*, 154·5) and 1-*bromo*-2-*chlorotetrafluoroethane* (68%), b. p. 25·5° (Found: C, 11·4%; *M*, 216. C_2ClBrF_4 requires C, 11·1%; *M*, 215·5). When shaken with zinc (5 g.) and ethanol (20 ml.) in a sealed tube at 80°, 1-bromo-2-chlorotetrafluoroethane (2·4 g.) was converted into tetrafluoroethylene (95%), identified spectroscopically. The ethanolic solution contained bromide and chloride (98%) in a ratio of 1·03 : 1·00. (*b*) Irradiation by a Hanovia lamp of mercury (10 ml.) and a solution of 1-bromo-2-chloro-1 : 1 : 2-trifluoroiodoethane (5·1 g.) in ethanol (3 ml.) and light petroleum (2 ml.; b. p. 100—120°) containing pyrogallol (0·2 g.) in a silica tube shaken vigorously and heated at 120—150° for 48 hours gave 1-bromo-2-chloro-1 : 1 : 2-trifluoroethane (53%), b. p. 52·8°, n_D^{25} 1·368 (Found: C, 12·1%; *M*, 196. Calc. for $C_2HClBrF_3$: C, 12·1%; *M*, 197·5). Park, Sharrah, and Lacher (*J. Amer. Chem. Soc.*, 1949, **71**, 2339) report b. p. 46°/619 mm. Treatment with zinc and ethanol removed bromine and chlorine (and no fluorine), in a 1 : 1 ratio, from 1-bromo-2-chloro-1 : 1 : 2-trifluoroethane, to give trifluoroethylene (91%), b. p. −55° (Found: *M*, 82. Calc. for C_2HF_3: *M*, 82), identified by infra-red spectroscopy. Swarts (*Bull. Acad. roy. Belg.*, 1899, **37**, 357) reports b. p. −51°.

After exposure to ultra-violet radiation for 8 hours in a silica tube, 1-bromo-2-chloro-1 : 1 : 2-trifluoroiodoethane (4·2 g.) and chlorine (100% excess) gave 1-*bromo*-2 : 2-*dichlorotrifluoroethane* (83%), b. p. 70—71° (Found: C, 10·6%; *M*, 232. $C_2Cl_2BrF_3$ requires C, 10·3%; *M*, 232). Similarly, photochemical bromination gave 1 : 2-dibromo-1-chlorotrifluoroethane, b. p. 92° (76%).

Conversion of 1-*Bromo*-2-*chloro*-1 : 1 : 2-*trifluoroiodoethane into Hexafluorobutadiene.*—Mercury (10 ml.) and 1-bromo-2-chloro-1 : 1 : 2-trifluoroiodoethane (16·2 g.) were sealed in a silica tube which was shaken vigorously and exposed to ultra-violet radiation for 3 days. The liquid products were separated from mercuric iodide by heating and pumping into a trap cooled in liquid air, and then distilled, to give 1 : 4-*dibromo*-2 : 3-*dichlorohexafluorobutane* (14·8 g., 75%), b. p. 75°/20 mm., n_D^{20} 1·427 (Found: C, 12·3; Br + Cl, 58·6. $C_4Br_2Cl_2F_6$ requires C, 12·2; Br + Cl, 58·8%), and unchanged 1-bromo-2- chloro-1 : 1 : 2-trifluoroiodoethane (<1%).

The 1 : 4-dibromo-2 : 3-dichlorohexafluorobutane (7·9 g.) dissolved in ethanol (10 ml.) was added as fast as possible to zinc powder (20 g.) in boiling ethanol (50 ml.); after 6 hours the volatile products were washed with water and fractionated *in vacuo*, to give hexafluorobutadiene (3·05 g., 92%), b. p. 5·5—6·0°, whose identity was confirmed by its infra-red spectrum.

Bromination and Chlorination of Hexafluorobutadiene.—Treatment of hexafluorobutadiene (4·0 g.) with a 5% excess of bromine at 120° with exposure to ultra-violet light gave 1 : 2 : 3 : 4-*tetrabromohexafluorobutane* (theoretical yield), b. p. 130°/70 mm., 105°/40 mm., *ca.* 210°/760 mm., n_D^{25} 1·464 (Found: C, 10·2; Br, 65·9. $C_4Br_4F_6$ requires C, 10·0; Br, 66·4%), reconverted into the diene by zinc and refluxing ethanol. Irradiation of the fluorodiene at room temperature with 1·0 mol. of bromine gave mixed dibromohexafluorobutenes, b. p. 99—100°, n_D^{25} 1·394, which on further reaction with bromine gave 1 : 2 : 3 : 4-tetrabromohexafluorobutane, identical with that described above; similarly, 1 mol. of chlorine was absorbed to give a mixture of dibromodichlorohexafluorobutanes. When the dibromohexafluorobutene mixture (4·31 g.) was added to zinc and refluxing dioxan, the yield of hexafluorobutadiene, identified spectroscopically, after 12 hours was 37%. The dioxan solution was freed from zinc by filtration, then treated with an excess of water, and the precipitated oil was dried, distilled, and heated at 40° with an excess of freshly prepared antimony trifluoride to which chlorine had been added (Sb^{III} : Sb^{V} = 1 : 1). The gaseous products, washed with 10% aqueous sodium hydroxide and distilled *in*

vacuo, gave octafluorobut-2-ene (49%, based on original mixture), identified by spectroscopic examination of the dibromide. When the above procedure was reversed, unchanged dibromohexafluorobutene being removed from the fluorinating agent by pumping and then subjected to treatment with zinc and dioxan, the yield of octafluorobut-2-ene was 41% and of hexafluorobutadiene was 44%.

When mixed with a 5% excess of dry chlorine in a silica vessel, heated to 40°, and exposed to ultra-violet radiation for 3 minutes, hexafluorobutadiene (3·1 g.) was converted quantitatively into 1 : 2 : 3 : 4-tetrachlorohexafluorobutane, b. p. 134°, shown by infra-red spectroscopy to be identical with that described earlier.

Hexafluorobutadiene (4·4 g.) and 50% of the chlorine required for saturation were condensed into a silica tube which, after being sealed and vigorously shaken, was exposed to ultra-violet radiation and allowed to warm to room temperature. Reaction was complete in 2 minutes, and gave unchanged hexafluorobutadiene (15%), 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (17%), and a mixture (61%) of 3 : 4-dichlorohexafluorobut-1-ene and 1 : 4-dichlorohexafluorobut-2-ene (b. p. 64·5—65·5°, n_D^{20} 1·341). Treatment of this mixture of chlorofluorobutenes with zinc and boiling ethanol gave hexafluorobutadiene (31%), and treatment with antimony trifluorodichloride gave octafluorobut-2-ene (61%). The mixture of chlorofluorobutenes absorbed chlorine quantitatively to give 1 : 2 : 3 : 4-tetrachlorohexafluorobutane, shown, by infra-red spectroscopy, to be identical with that described above; it absorbed bromine quantitatively to give a mixture of dibromodichlorohexafluorobutanes converted into hexafluorobutadiene by zinc and refluxing ethanol.

Since the above work was complete, Miller (*op. cit.*) has listed compounds prepared by his group by alternative unpublished procedures. These include $(CClF_2{\cdot}CClF)_2$, b. p. 134·5—134·6°/700 mm., n_D^{20} 1·3853; $(CBrF_2{\cdot}CBrF)_2$, b. p. 118—122°/60 mm., n_D^{20} 1·467, $(CF_3{\cdot}CBrF)_2$, b. p. 96°, n_D^{20} 1·3574; and $(CClF_2{\cdot}CF_3)_2$, b. p. 64—66°.

Absorption Spectra.—Silica gas cells (10 cm. and 4 cm.) were used and the extinction coefficient, ε, was calculated from the equation $\varepsilon = 760\,D \times 22{\cdot}4 \times 290/273pl$ where D = optical density, p = gas pressure (mm.), and l = cell length (cm.). No great accuracy is claimed for the ε values of hexafluorobutadiene, owing to possible errors in measuring the low pressures required.

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850. *The System* $Al_2(SO_4)_3$–H_2SO_4–H_2O.

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Improved analytical methods being used, the system $Al_2(SO_4)_3$–H_2SO_4–H_2O has been investigated by phase-rule methods at 25°, 30°, 50°, and 60°, and the following solid phases have been found: $Al_2(SO_4)_3{,}16H_2O$, which habitually contains about half a molecule of additional water held by adsorption or in a zeolitic manner; $Al_2(SO_4)_3{,}14H_2O$; $2Al_2(SO_4)_3{,}H_2SO_4{,}24H_2O$; $Al_2(SO_4)_3{,}H_2SO_4{,}12H_2O$; $Al_2(SO_4)_3{,}H_2SO_4{,}8H_2O$ in two forms, the metastable one of which contains a slight excess of acid; $Al_2(SO_4)_3{,}H_2SO_4{,}2H_2O$, which contains a slight excess of acid and water. Anhydrous $Al_2(SO_4)_3$ with and without a slight excess of acid and water, $Al_2(SO_4)_3{,}H_2SO_4{,}2H_2O$, $Al_2(SO_4)_3{,}9H_2O$, and $Al_2(SO_4)_3{,}6H_2O$ have been prepared in other ways. All these solids have been isolated in the dry state for analysis, and in a search for isomorphism their *X*-ray powder photographs have been compared with those of the mineral coquimbite, of corresponding ferric sulphates, and of ferric ammonium sulphate and its tetrahydrate. Solubilities, microscopical appearances, and lattice spacings are recorded. The nature of the non-stoicheiometric solid phases and the application of Taylor's criteria (*J.*, 1952, 2370) for distinguishing between normal and acid sulphates are discussed. Certain results for the $Al_2(SO_4)_3$–H_2O system are included.

THE investigation by phase-rule methods of systems of the type metal sulphate–sulphuric acid–water can furnish valuable data regarding the hydrates of the metal sulphate and the occurrence of acid sulphates (cf. Taylor, *J.*, 1952, 2370). In the case of aluminium sulphate, 13 hydrates of the normal sulphate containing from 2 to 27 molecules of water of crystallisation, together with six acid sulphates varying from 1,1,3

[$\equiv Al_2(SO_4)_3,H_2SO_4,3H_2O$, a convention which is used throughout this paper] to 1,3,12 have been reported, but it seems very doubtful if all of these are in fact distinct chemical individuals, and furthermore, little information is available regarding the conditions under which they are stable (Mellor, " Inorganic and Theoretical Chemistry," Longmans, 1924, **5**, p. 332). Recent ternary solubility work has failed to clarify this position. Henry and King (*J. Amer. Chem. Soc.*, 1949, **71**, 1142) have reported a complete isotherm at 60° showing the four solid phases $Al_2(SO_4)_3,16H_2O$, $Al_2(SO_4)_3,9H_2O$, 1,3,12, and $Al_2(SO_4)_3$, the one succeeding the other as the acid concentration increased. Collet (*Compt. rend.*, 1950, **230**, 951) has reported the following sequence at 20° : the 18-, 16-, 10-, and 6-hydrates of the normal sulphate followed by 1,1,4; while Funaki (*Bull. Tokyo Inst. Tech.*, 1950, Series B, No. 1, 66) has claimed the sequence 18-, 16-, 9-hydrates followed by 1,5,0 at 25°. On the other hand, very careful work by Bassett and Goodwin (*J.*, 1949, 2239) has shown that at 25° up to an acid concentration of 47·5% only the 16-hydrate of the normal sulphate occurs as stable solid phase.

In an attempt to clarify this situation, a full investigation of the ternary system from 25° to 60° was undertaken and also of some features of the $Al_2(SO_4)_3$–H_2O system. Certain aspects of the corresponding ferric sulphate system have also been examined and a comparison of the two has helped to elucidate some features of the aluminium sulphate system. For the latter, it is of prime importance that the solubility determinations should be of the highest possible accuracy, for in assessing tie-line convergence points on the usual triangular diagram quite small errors assume major significance. This arises in view of the large molecular weight of aluminium sulphate compared with those of water and sulphuric acid. All techniques and analytical procedures were therefore the subject of special investigation.

Preliminary results have already been reported by Taylor and Scott (*Nature*, 1951, **168**, 520) who (*a*) have shown by tracer technique, using radioactive cæsium sulphate and manganese sulphate as tracers, that the salt of composition 1,1,12 occurs as a stable phase in the 30—50° range, and (*b*) reported the occurrence of 1,1,8 (in two forms) and 1,1,2.

Experimental

Materials.—Wherever possible the reagents were of " AnalaR " grade. The aluminium sulphate was recrystallised by Smith's procedure (*J. Amer. Chem. Soc.*, 1942, **64**, 41) and dried in air overnight at room temperature. The resulting product was perfectly dry, neither deliquesced nor effloresced under ordinary atmospheric conditions, and dissolved completely in distilled water. Sodium and potassium salts, the most likely impurities, were shown to be present only in minute traces even in the unrecrystallised salt. For all solubility determinations at low acid concentrations the recrystallised salt was used; at high acid concentrations, the unrecrystallised material was used. The latter was justified by (*a*) the absence of impurities in the " AnalaR " salt apart from very small amounts of basic sulphate, (*b*) the agreement of solubility results when either material was used, and (*c*) the rapid conversion under highly acid conditions of any basic sulphate present. Different preparations of the recrystallised material contained between 16·5 and 16·8 molecules of water of crystallisation and no free acid. Ferric sulphate (B.D.H.) was used without further purification. It was shown by the procedure below to have the approximate composition 5,2,29, and an *X*-ray powder photograph showed that the majority of the acid was present as the 1,1,2 salt.

Methods of Analysis.—In all cases, the metal and either the total SO_4 radical or the free acid concentration were determined, the water being obtained by difference.

Aluminium was determined by precipitation with 8-hydroxyquinoline using a modification of Cumming and Kay's procedure (" Quantitative Chemical Analysis," Gurney and Jackson, 9th edn., 1945, p. 284). The greater part of any sulphuric acid present was neutralised with ammonia and the temperature raised to 90—95° before dropwise addition of the ammonium acetate solution. This avoided inconveniently large volumes of ammonium acetate and conferred a slightly improved physical form on the precipitate such that sintered-glass crucibles of grade 3 porosity could be used with confidence. With precipitates of less than 0·2 g., it was essential to cool slowly to room temperature before filtration, otherwise results were up to 2% low. Precipitates were washed with water at 30—40° and dried to constant weight at 120°. This procedure proved accurate for several total weights of aluminium sulphate and various acid : salt ratios, a Hilger high-purity sample of aluminium (99·98% pure) being used as standard.

The results recorded in Table 1 cover the actual concentration conditions encountered in solutions from solubility measurements.

TABLE 1. *Determination of aluminium.*

Taken	$Al_2(SO_4)_3$, g.	0·0326	0·0326	0·0816	0·1630
	Wt. ratio, $H_2SO_4 : Al_2(SO_4)_3$	300	100	5	5
Found: $Al_2(SO_4)_3$, g.		0·0333	0·0327	0·0816	0·1628

Total sulphate was determined by direct precipitation with barium chloride without removal of aluminium. In accord with the results of Bassett and Goodwin (*loc. cit.*), no adsorption of aluminium on the barium sulphate precipitate (leading to low results) was observed, and distinct loss of sulphate occurred if the aluminium was previously removed by precipitation (and even re-precipitation) with ammonia. Some trouble arose from the poor physical form of the precipitate, and although the use of picric acid effected a moderate improvement, a complete remedy apart from the inadmissible removal of the aluminium was not found. Subsequently, a more rapid volumetric procedure for free sulphuric acid was developed from the method given by Scott and Furman ("Standard Methods of Chemical Analysis," Technical Press Ltd., 5th edn., 1939, p. 16), in which the sulphuric acid is titrated with alkali after addition of potassium fluoride to precipitate the aluminium as $AlF_3,3KF$. Experiment showed that this procedure gave results which were up to 3% low depending on the ratio $H_2SO_4 : Al_2(SO_4)_3$, the loss of acid being due presumably, as suggested by Graham (*Ind. Eng. Chem. Anal.*, 1946, **18**, 472), to its adsorption on the complex fluoride precipitate. To avoid this loss in special cases where the ratio $H_2SO_4 : Al_2(SO_4)_3$ was very high, Graham recommended delaying the addition of the fluoride until after 99·5% of the acid had been neutralised (cf. Glemser and Thelen, *Angew. Chem.*, 1950, **62**, 269), but the present research showed that in all cases virtually

TABLE 2. *Determination of* H_2SO_4 *in presence of* Al.

Taken			Found: *				Found: †
H_2SO_4, ml. 0·905N	$Al_2(SO_4)_3$, g.	Wt. ratio, $H_2SO_4 : Al_2(SO_4)_3$	NaOH ml. 0·481N	H_2SO_4, ml. 0·905N	$Al_2(SO_4)_3$, g.	Wt. ratio, $H_2SO_4 : Al_2(SO_4)_3$	NaOH, ml. 0·0993N
10·0	0·0	—	18·83	1·00	0·0	—	9·12
10·0	0·027	16	18·82	1·00	0·25	0·17	9·15
10·0	0·160	3	18·82	1·00	0·85	0·05	9·12
10·0	0·424	1	18·82				

* Calc.: 18·82 ml. † Calc.: 9·11 ml.

the complete neutralisation of the acid before addition of the fluoride was essential. A series of titrations was always carried out in which progressively larger amounts of alkali were added before the fluoride until no further increase in titre was observed. The results in Table 2 show this procedure to be reliable.

Repeated comparison of the oxine–barium sulphate and volumetric methods for free acid determination showed that they agreed to 2 parts in 1000 except when both the free acid concentration and the acid : salt ratio were low. In this range, the volumetric method gave results up to 3% higher, and is considered more accurate for it gives the acid concentration directly instead of as a small difference between two large quantities both of which may contain an experimental error.

Ferric sulphate compounds were analysed for iron either by direct ignition with blowpipe heating to ferric oxide or by reduction with aluminium followed by permanganate titration (Cumming and Kay, *op. cit.*, p. 395). Total SO_4 radical was determined by titration at the boil with sodium hydroxide to phenolphthalein end-point.

Ternary Solubility Measurements.—Solubility determinations were carried out in a manner analogous to that given by Taylor (*loc. cit.*) with the addition that all initial solids by careful heating were brought completely into solution before being stirred to equilibrium. Certain mixtures at very high acid concentrations required the use of oleum in place of "AnalaR" sulphuric acid. The time to attain equilibrium varied from a few hours at the low-acid side to several months at the high-acid side of the system. Seeding with the desired solid phase was frequently advantageous, and occasionally after the desired solid phase had been obtained from a mixture of known composition, the latter was adjusted to a different value by the addition of water or acid as required. Nevertheless, stubborn metastability was frequently encountered, particularly at high acid concentrations. At equilibrium, mixtures were filtered with suction either through a sintered-glass micro-filter stick of No. 3 porosity attached to a pre-heated pipette, or through a number 3 grade sintered-glass mercury filter suitably attached to a small receiver. The

open end of the mercury filter could be closed with a calcium chloride tube, and the whole unit immersed in the thermostat so that the very slow filtering mixtures encountered at the high acid side of the system could be filtered without disturbance of the equilibrium. After filtration, weighed samples of the solution and moist solids were diluted to a standard volume and analysed. Continuous use was made of microscopical examinations and of *X*-ray powder photographs in

TABLE 3. *The system* $Al_2(SO_4)_3$–H_2SO_4–H_2O.

Solution: $Al_2(SO_4)_3$, %	Solution: H_2SO_4, %	Moist solid phase: $Al_2(SO_4)_3$, %	Moist solid phase: H_2SO_4, %	Solid phase		Solution: $Al_2(SO_4)_3$, %	Solution: H_2SO_4, %	Moist solid phase: $Al_2(SO_4)_3$, %	Moist solid phase: H_2SO_4, %	Solid phase
				At 25°						
27·76	0·0	—	—	A		* 1·42	68·68	17·74	51·46	B
27·74	0·0	—	—	A		0·67	65·66	23·73	43·69	B + C
27·79	0·0	—	—	A		0·23	68·36	15·16	55·16	C
23·89	4·78	38·59	2·48	A		0·59	69·32	20·27	51·77	C
16·88	14·60	36·76	6·67	A		0·18	73·20	13·05	61·13	C
5·23	36·12	29·93	17·58	A		0·19	73·93	—	—	C
3·19	45·26	26·47	24·28	A		0·57	78·13	—	—	C
3·05	45·99	30·31	21·54	A		* 0·77	79·77	16·70	62·41	C
3·14	47·30	—	—	A		* 1·08	80·25	14·11	65·80	C
3·13	47·53	24·77	27·16	A		†† 0·6	78·5	—	—	C + E
3·22	48·30	24·33	30·50	A + B		** 1·12	72·61	37·85	37·26	D
2·50	49·55	27·98	31·61	B		* 0·36	74·60	—	—	D
2·46	50·10	24·28	33·81	B		* 0·37	74·60	37·98	38·50	D
0·95	56·21	14·73	44·54	B		** 1·31	75·33	30·97	44·65	D
0·75	58·10	27·11	35·74	B		0·18	82·49	30·39	57·00	E
0·62	58·89	20·78	41·43	B		0·12	83·90	—	—	E
0·56	63·48	16·32	48·33	B		0·14	86·48	25·72	63·17	E
0·64	65·32	17·50	48·44	B		† 0·01	92·71	7·62	85·09	E
* 0·68	66·20	—	—	B		<0·07	99·30	—	—	E
				At 30°.						
3·98	45·24	—	—	A		3·01	49·71	—	—	B
4·36	46·86	§ 51·25	14·12	A + B		0·93	57·89	38·35	26·75	B
4·06	47·50	—	—	B						
				At 50°.						
29·70	0·0	—	—	A		3·29	52·41	—	—	G
25·53	5·28	—	—	A		†† 3·30	53·90	—	—	G + B
20·57	13·22	—	—	A		* 3·81	52·53	—	—	B
11·67	31·27	—	—	A		* 3·48	53·61	—	—	B
10·02	36·41	—	—	A		3·27	54·20	—	—	B
* 9·91	39·65	34·87	17·64	A		2·27	59·03	—	—	B
* 9·90	40·36	—	—	A		* 2·22	61·31	—	—	B
†† 10·0	37·0	—	—	A + F		†† 2·20	60·00	—	—	B + C
8·93	39·40	—	—	F		0·77	64·90	—	—	C
†† 8·2	41·5	—	—	F + G		0·43	72·70	—	—	C
* 9·91	38·90	—	—	A + G		0·71	76·73	—	—	C
7·82	42·08	—	—	G		* 1·33	78·43	—	—	C
7·47	42·60	—	—	G		†† 0·80	77·00	—	—	C + E
6·16	44·94	—	—	G		0·07	83·00	—	—	E
5·61	46·26	49·23	14·40	G		<0·07	92·50	—	—	E
3·54	51·40	40·29	22·60	G						
				At 60°.						
* 14·82	31·56	—	—	A		* 12·44	36·95	—	—	G
* 14·43	33·91	—	—	A		* 11·44	38·39	—	—	G
†† 14·3	34·4	—	—	A + G		* 10·31	40·11	—	—	G
†† 17·0	25·5	—	—	A + F		* 9·21	42·09	—	—	G
12·56	32·80	—	—	F		6·76	46·61	—	—	G
10·18	37·45	—	—	F		†† 4·7	54·5	—	—	G + B
9·59	39·23	—	—	F		* 6·52	49·74	—	—	B
† 8·00	44·00	—	—	F + G		* 5·27	52·43	—	—	B
* 12·62	36·60	—	—	G		3·96	57·53	—	—	B

* = Metastable. ** = May be supersaturated. † = Al estimated colorimetrically with alizarin.
†† = Interpolated invariant points. § = Acetone-washed dry solids.

Solid phases:
A = $Al_2(SO_4)_3.16H_2O$.
B = $Al_2(SO_4)_3.H_2SO_4.12H_2O$.
C = $Al_2(SO_4)_3.H_2SO_4.8H_2O$, stable form.
D = $Al_2(SO_4)_3.H_2SO_4.8H_2O$, metastable form.
E = " acidic " $Al_2(SO_4)_3.H_2SO_4.2H_2O$.
F = $Al_2(SO_4)_3.14H_2O$.
G = $2Al_2(SO_4)_3.H_2SO_4.24H_2O$.

Further details are given on pp. 4434—4438.

recognising solid phases and invariant points and particularly in following the course of solid phase transitions. Results are given in Table 3 and Figs. 1 and 2. The position of all tie-lines was determined with the aid of mathematical extrapolation to eliminate drawing errors. Compositions are by weight.

FIG. 1. *System* $Al_2(SO_4)_3$–H_2SO_4–H_2O *at* 25°.

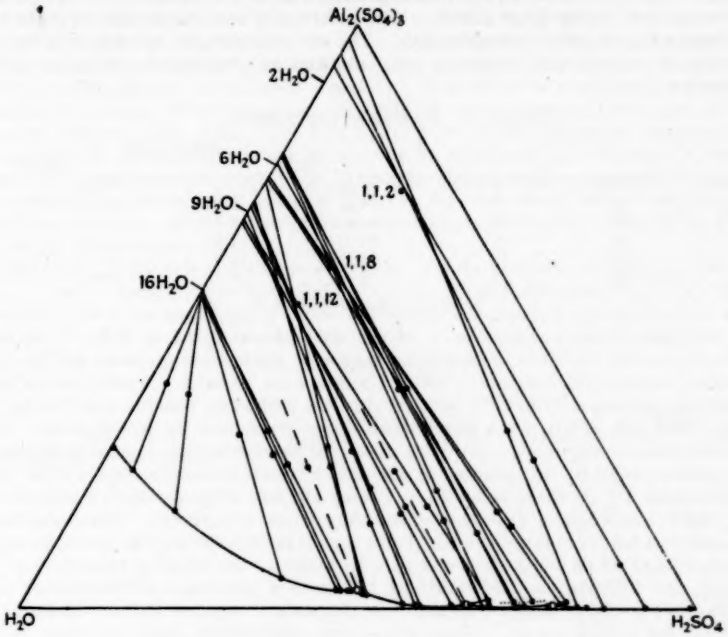
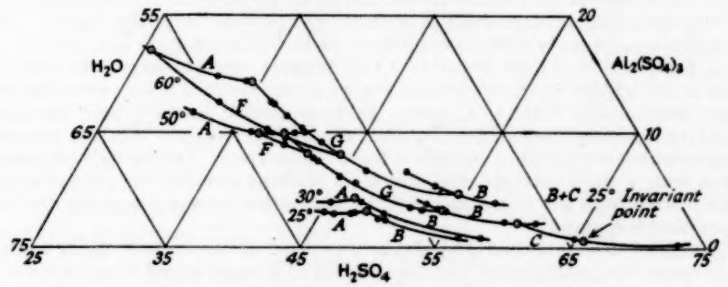


FIG. 2. *System* $Al_2(SO_4)_3$–H_2SO_4–H_2O at 25°, 30°, 50°, *and* 60°



Solid phases indicated by capital letter as in Table 3.
Open circles denote isothermal invariant points.

Indicator Experiments in the Ternary System.—Three indicators were used: radioactive cæsium sulphate, manganese sulphate, and hydrogen chloride. Details for the radioactive tracer work at 30° have been given elsewhere (Taylor and Scott, *loc. cit.*), and the manganese (one drop of 30% sulphate solution per 50 g. of ternary mixture) was used in essentially the same manner at 25°, the indicator being determined colorimetrically as permanganate after oxidation with potassium periodate in presence of phosphoric acid (Cumming and Kay, *op. cit.*, p. 270). It was essential to add the manganese sulphate after the ternary mixture had been brought to equilibrium, otherwise the manganese was completely co-precipitated with the solid phase. In addition to experiments on acidic solid phases, a test of the whole procedure was carried out

with a mixture known to contain $Al_2(SO_4)_3,16H_2O$ as solid phase, the free acid concentration being about 46%, *i.e.*, as high as conveniently possible without causing the solid to be transformed into 1,1,12. Experiments at very high acid concentrations were unsuccessful owing partly to precipitation of the indicator and partly to its adsorption on the very finely divided solid phases occurring at such acid concentrations. In the case of hydrogen chloride at 25°, the indicator was added at the outset and determined after equilibrium was reached by electrometric titration with N/100-silver nitrate. The presence of aluminium and sulphate was shown not to influence the chloride determination. The use of hydrogen chloride was limited by its low solubility in concentrated sulphuric acid solutions at atmospheric pressure. Results are given in Table 4.

TABLE 4. *Indicator experiments.*

			Composition: Calc.:		Found:	
Indicator	Temp.	Solid phase	$Al_2(SO_4)_3$, %	H_2SO_4, %	$Al_2(SO_4)_3$, %	H_2SO_4, %
$MnSO_4$	25°	A	54·3	0·0	58·4	−3·7
Cs_2SO_4	30	B	52·1	14·9	51·3	15·9
$MnSO_4$	25	B	52·1	14·9	51·5	15·1
HCl	25	B	52·1	14·9	48·1	17·8
$MnSO_4$	25	D	58·5	16·8	55·5	21·6

Solid phases as in Table 3.

Pure Dry Solid Phases.—Samples of all the solid phases listed in Table 3, together with several others not directly encountered in the solubility work, were prepared and analysed, and *X*-ray powder photographs were taken with a Unicam 9-cm. camera. A number of similar ferric compounds, whose compositions have been reliably established by Posnjak and Merwin (*J. Amer. Chem. Soc.*, 1922, **44**, 1965), were also prepared and examined for isomorphism with corresponding aluminium compounds. In cases involving the separation of a solid from a mother-liquor the simple procedure was adopted of washing the moist solids thoroughly with " AnalaR " acetone containing 1% of water, followed by drying at room temperature in a current of dry air and finally for five minutes at a pressure of less than 1 mm. of mercury. Microscopical appearances are recorded below, compositions in Table 5, and lattice spacings in the Appendix.

$Al_2(SO_4)_3,16H_2O$ (*A in Tables* 3, 4 *and* 5). As a test of the washing procedure in removing acidic liquid, the hydrate was separated at 25° from a saturated mother-liquor containing approximately 46% of free acid. The resulting dry solid contained 16·2 molecules of water of crystallisation and zero free acid. When grown very slowly from dilute solution, the hydrate was obtained as extremely thin elongated hexagons with vertical angle 92° 40′ (cf. Delacharlonny, *Compt. rend.*, 1883, **96**, 844) and symmetrical extinction, but in solubility experiments the usual habit was long thin laths extinguishing at an angle of about 43° with the length. The lattice spacings corresponded exactly with those given by Bassett and Goodwin (*loc. cit.*).

$Al_2(SO_4)_3,14H_2O$ (*F in Tables* 3 *and* 5). This hydrate was obtained only from solubility experiments at 50° and 60°, and was formed always as the result of a very slow transformation of either the 16-hydrate or the 2,1,24 phase. Its precipitation from solutions metastable with respect to 2,1,24 was sometimes assisted by addition of a little water. Washing was with warm acetone, the resulting solid containing only a trace of free acid. The crystals occurred as long narrow laths with a single oblique end-face, some showing parallel extinction and some not. It was distinguished from the 16-hydrate most reliably either by analysis of the dry solid or by its *X*-ray powder photograph.

$Al_2(SO_4)_3,9H_2O$. Recrystallised 16-hydrate was dried in air at 100° till it contained 8·7 molecules of water of crystallisation and then heated in a small sealed Pyrex tube at 160° for 9 weeks, during which time the solid underwent a visible recrystallisation. *X*-Ray powder photographs showed that the solid was practically structureless before heating but gave a characteristic diagram afterwards, such that the crystals obtained are thought to be essentially the 9-hydrate. They were highly birefringent, biaxial positive, with irregular shapes.

$Al_2(SO_4)_3,6H_2O$. This was prepared in the same way as the 9 hydrate starting from an amorphous solid containing 6·7 molecules of water of crystallisation. Small birefringent needles with oblique extinction were obtained which gave a good *X*-ray diagram.

Anhydrous $Al_2(SO_4)_3$. Heating of recrystallised 16-hydrate in air at 500° for 150 hours gave a product which analysis showed to be $Al_2(SO_4)_3$ apart from a slight loss of SO_3 and a very little residual water. The *X*-ray diagram showed the product to be well crystallised.

" *Acidic*" *anhydrous* $Al_2(SO_4)_3$. By dissolving 3 g. of "AnalaR" salt in 25 ml. of 70—80% acid and gently boiling the solution till fuming occurred, small thin hexagonal plates were first

precipitated (see below under 1,1,2), which on further heating were transformed into dense birefringent small square tablets (*d* 2·7). Although the *X*-ray diagram was identical with that of anhydrous $Al_2(SO_4)_3$, the square tablets contained about 1% of water and 7% of free acid. The presence of the latter on the surface of the crystals would indicate failure of the acetone washing procedure but this was shown not to be the case as follows. After immersion of the tablets in distilled water with intermittent stirring for 10 minutes and filtering, the filtrate contained only 15% of the free acid present in the crystals and a small quantity of aluminium ion. Furthermore, although the excess of acid varied a little from one preparation to another, yet it was independent of the volume of wash liquid.

$2Al_2(SO_4)_3,H_2SO_4,24H_2O$ (*G in Tables* 3 *and* 5). This phase was obtained as well-formed 0·5-mm. six-sided plates, biaxial negative, in solubility experiments at 50° and 60° by slow transformation of previously precipitated 16-hydrate or 1,1,12, and over appreciable ranges remained metastable with respect to the 14-hydrate for long periods. Whether it was isolated by acetone or by absolute alcohol washing, the composition was the same and the dry crystals appeared completely unchanged. Although the two tie-lines could indicate a composition of 2,1,22, analyses for three different preparations were very close to the composition 2,1,24, and the latter is therefore preferred.

$Al_2(SO_4)_3,H_2SO_4,12H_2O$ (*B in Tables* 3, 4, *and* 5). Crystals of this composition were obtained very easily at all temperatures in the solubility work. The habit was small, very thin, birefringent plates, almost square, many of which had one or both pairs of opposite corners truncated.

TABLE 5. *Dry solid phases.*

Temp. of preptn.	Solid phase	Composition: Calc.: $Al_2(SO_4)_3$, %	Calc.: H_2SO_4, %	Found: $Al_2(SO_4)_3$, %	Found: H_2SO_4, %
Aluminium sulphate compounds.					
25°	A	54·3	0·0	53·16	0·0
				53·41	0·0
				54·00	0·0
60	F	57·57	0·0	58·23	<0·2
				58·29	<0·1
				57·20	<0·1
25	B	52·1	14·94	51·45	15·02
50	B	52·1	14·94	51·29	15·36
				51·41	15·14
50	G	56·30	8·07	56·51	8·63
				56·47	8·48
				56·20	8·39
25	C	58·50	16·78	57·24	18·01
50	C	58·50	16·78	58·19	17·42
25	D	58·50	16·78	57·35	17·91
				56·20	18·84
				56·36	18·92
25	E	71·9	20·6	63·97	23·28
				64·85	23·20
				64·80	22·29
50	E	71·9	20·6	67·20	24·08
~190	1,1,2	71·9	20·6	71·15	20·38
~300	" Acidic " anhyd.	100·0	0·0	91·31	7·88
				93·27	5·87
500	Anhydrous	100·0	0·0	100·9	−2·57
		Solid phases as in Table 3.			
Ferric sulphate compounds.		$Fe_2(SO_4)_3$, %	H_2SO_4, %	$Fe_2(SO_4)_3$, %	H_2SO_4, %
25	8-Hydrate	73·52	0·0	73·0	0·08
25	1,1,8	62·27	15·28	62·6	14·5
50	1,1,2	74·87	18·36	74·4	17·67
~300	Anhydrous	100·0	0·0	99·98	0·0

$Al_2(SO_4)_3,H_2SO_4,8H_2O$, *Stable form* (*C in Tables* 3 *and* 5). Several days' stirring were required even with seeding to induce precipitation of this solid as extremely small birefringent needles.

$Al_2(SO_4)_3,H_2SO_4,8H_2O$, *Metastable form* (*D in Tables* 3, 4, *and* 5). At 25° in the middle of the 1,1,8 range, a metastable form was obtained in quantity provided the solution initially was highly supersaturated; from less supersaturated solutions both forms frequently appeared

together. The crystals were in the form of rectangular blocks with bevelled end-faces, biaxial positive, a habit which was completely unchanged after acetone washing. The composition of different preparations varied slightly, having 1—2% of acid in excess of the composition 1,1,8. Doubling the quantity of wash liquid did not alter the composition. The crystals proved too unstable in air to give a reliable *X*-ray diagram, but a photograph of a mush of crystals and mother-liquor gave sufficient spacings to show that the two forms probably had different structures.

$Al_2(SO_4)_3,H_2SO_4,2H_2O$. The hexagonal plates referred to on p. 4436 in the preparation of "acidic" anhydrous $Al_2(SO_4)_3$ gave analyses very close to the composition 1,1,2. The hexagons were regular and isotropic normal to the six-fold axis, and the crystals thus belong to the hexagonal class. Observations during six months showed that transition to the square tablets phase did not occur below about 200°.

"*Acidic*" $Al_2(SO_4)_3,H_2SO_4,2H_2O$ (*E in Tables* 3 *and* 5). From supersaturated solutions containing more than 80% of free acid, small, roughly spherical, random aggregates of birefringent crystals were precipitated on prolonged stirring. Although these aggregates contained several units % more sulphuric acid and water (quantities which varied slightly from one preparation to another) than 1,1,2, the *X*-ray powder photographs were very similar, showing that both substances had essentially the same lattice structure. The composition was not dependent on the volume of wash-liquid used.

Alunite. About 2% of the 9-hydrate preparation was very slow to dissolve in boiling dilute sulphuric acid. This residue, after-being washed with water and dried (P_2O_5) in a desiccator, was found to have an *X*-ray powder photograph characteristic of the alunite group. It contained only Al and SO_4 apart from water and may therefore have the composition $H_2O[Al_3(OH)_6H_2O](SO_4)_2$, which is one member of the alunite series (Bassett and Goodwin, *loc. cit.*; Bassett, *J.*, 1950, 1460).

Coquimbite. A Royal Scottish Museum specimen, number 1875/9/9, was made available through the kind co-operation of Dr. C. D. Waterston. With assistance from Mr. A. R. Chalmers, the mineral was shown to have the composition $Fe_{1\cdot54}Al_{0\cdot46}(SO_4)_3,9H_2O$.

$Fe_2(SO_4)_3,8H_2O$. From a saturated solution containing 2—3% of free acid, after partial evaporation over phosphoric oxide followed by several days' stirring at 25°, minute fawn needles were obtained. After filtration, the hydrate was washed with a few drops of ice-cold water and then with acetone. It was found that transition to the 1,1,8 compound commenced in solution at a free acid concentration of about 5%, which is contrary to the published data (collected refs. in Seidell, "Solubilities of Inorganic and Metal Organic Compounds," Van Nostrand, 3rd edn., 1940).

TABLE 6. *The system* $Al_2(SO_4)_3$–H_2O [solid phase: $Al_2(SO_4)_3,16H_2O$].

Temp., °c	50·5	73·4	75·0	76·7	82·9	88·0	95·1	99·2	103·2	110·4	112·2
Solution: $Al_2(SO_4)_3$, %	30·09	33·33	33·63	34·28	36·60	38·74	41·86	43·90	46·85	52·0	53·0

$Fe_2(SO_4)_3,H_2SO_4,8H_2O$. Baskerville and Cameron's phase equilibria data (*J. Phys. Chem.*, 1935, **39**, 769) being used, pale fawn six-sided plates were obtained at 25°. They were biaxial with the acute bisectrix almost perpendicular to the plane of the crystal.

$Fe_2(SO_4)_3,H_2SO_4,2H_2O$. Very irregular fawn birefringent plates were obtained at 50°, Posnjak and Merwin's phase data (*loc. cit.*) being used.

Anhydrous $Fe_2(SO_4)_3$. Pale fawn, square and rectangular tablets, some with extra faces, were obtained by boiling 2 g. of B.D.H. ferric sulphate in 20 ml. of 80% acid till the mixture fumed very strongly. The anhydrous compound was found to be the only equilibrium solid phase under such conditions (cf. Posnjak and Merwin, *loc. cit.*).

$(NH_4)_2SO_4,Fe_2(SO_4)_3$. This was prepared as well-formed nearly colourless hexagonal plates by low-temperature dehydration of ferric alum, and its composition checked by analysis.

$(NH_4)_2SO_4,Fe_2(SO_4)_3,4H_2O$. This was obtained as pale violet, tetragonal bipyramids by crystallisation at 25—30° of a solution of ferric alum strongly acidified with sulphuric acid. This *compound* does not appear to have been recorded previously [Found: Fe_2O_3, 26·4; $(NH_4)_2O$, 8·7; SO_3, 52·7. $(NH_4)_2SO_4,Fe_2(SO_4)_3,4H_2O$ requires Fe_2O_3, 26·4; $(NH_4)_2O$, 8·6; SO_3, 53·0%. The mother-liquor contained 4·5, 1·6, and 33·4%, respectively].

With the exception of the metastable aluminium 1,1,8 compound which dissolved readily, all solid phases with 9 or less molecules of water of crystallisation dissolved in water extremely slowly. Coquimbite and $Fe_2(SO_4)_3,8H_2O$ hydrolysed in water with the formation of a brown precipitate, but dissolved readily and completely in dilute acid.

Some Features of the $Al_2(SO_4)_3$–H_2O *System.*—(1) In a search for lower hydrates, solubility experiments by the synthetic method (cf. Taylor and Vincent, *J.*, 1952, 3218) were carried out in sealed tubes. Up to 112·2° (Table 6) the solid phase was the 16-hydrate and this probably just fails to have a congruent m. p. Above 112° two different solid phases appeared, but results were so erratic owing to the extreme slowness with which equilibrium was established in the highly viscous solutions that no estimate of the composition of the new phases could be made. At a composition corresponding to the 12-hydrate, the temperature of complete solution was about 200°. Since the 16-hydrate is only just able to give a congruent solution at 25°, and since hydrolysis may be expected to increase with rising temperature, some of the solutions in Table 6 may have been metastable with respect to a basic salt.

(2) At 25°, measurement of dissociation pressures, a McBain–Bakr silica spring balance and mercury manometer in an all-glass vacuum system being used, confirmed (*a*) the occurrence of the 14-hydrate, and (*b*) the ability of the 16-hydrate to absorb up to 0·8 molecule of water without the appearance of a liquid phase. The dissociation pressure for the reaction 16-hydrate $\rightleftharpoons$ 14-hydrate + $2H_2O$ was 10·5 mm. of mercury, and the vapour pressure of saturated aluminium sulphate solution 21·3 mm. For hydrates containing less than 14 molecules of water, dissociation pressures are less than 3 mm.

(3) Orthobaric dehydration of the 16-hydrate in air saturated at 25° with water vapour (cf. Milligan and Weiser, *J. Phys. Chem.*, 1934, **38**, 513) confirmed the observations made in (2) above, but gave no information regarding hydrates lower than 14 owing to the prohibitive time to reach equilibrium.

Discussion

The stable solid phase up to moderate acid concentrations in the 25—60° range is normal aluminium sulphate containing between 16 and 17 molecules of water of crystallisation. This phase is best regarded as a true 16-hydrate with the extra approximate 0·5 H_2O held by adsorption or in a zeolitic manner because (*a*) there is no evidence from any section of the work for a 16·5 $\longrightarrow$ 16-hydrate transition, and (*b*) the system solid 16-hydrate–water vapour was observed to be univariant over the composition range from 16 to 16·8 molecules of water per molecule of aluminium sulphate in the isothermal and orthobaric dehydration experiments. As far as tie-lines are concerned, the extra water is indistinguishable from true water of crystallisation and may therefore be held by relatively strong forces. This view is further supported by the facts that the extra water is invariably present in the solid no matter what its source, and the hydrate is not efflorescent in air.

In spite of the attention given to all analytical procedures, Fig. 1 shows that, with the exception of the 16-hydrate, the tie-line information, although clearly differentiating one solid phase from another, gave little more than suggestions as to their composition: following the 16-hydrate, a succession of highly hydrated acidic phases was favoured, but a sequence of lower hydrates of the normal sulphate was not ruled out. Recourse was therefore made to (1) indicator experiments, (2) isolation and analysis of dry solid phases, and (3) establishment by *X*-ray methods of isomorphism with corresponding ferric compounds of known composition.

The severe conditions which the ideal indicator in phase equilibria work must fulfil have been outlined by Taylor and Scott (*loc. cit.*), and it is seldom that such experiments yield more than suggestions as to solid-phase compositions. The unusual success with radioactive cæsium sulphate and manganese sulphate was due to both the minute quantity required and the accuracy with which they could be detected. Their use showed very definitely (Table 4) that phase B had the composition 1,1,12. The result for the hydrogen chloride indicator was less definite, but even so the acidic nature of the solid phase was clearly suggested. For the metastable phase D, manganese being used as indicator, the preferred composition was again that of 1,1 acidic solid. The fact that an experiment on the 16-hydrate with manganese as indicator definitely showed the absence of free acid from the solid phase, confirmed that the indicator procedure was trustworthy.

In the absence of radioactive indicator experiments at high acid concentrations, and the failure of the manganese and hydrogen chloride indicators under such conditions, attempts were made by washing with acetone to isolate all the solid phases including the ferric com-

pounds in the dry state for analysis. Such a procedure involves the possibility of (*a*) decomposition by loss or gain of water, acid or solvent, and (*b*) precipitation of unwanted solids from the mother-liquor. Point (*a*) is considered unimportant since (1) both the 16-hydrate and the 1,1,12 phase after isolation had compositions very close to those required by their formulæ, (2) the crystal habit of several of the phases appeared unchanged after the washing procedure, and (3) compositions were independent of the volume of wash liquid used. Furthermore, a number of the phases in Table 5 have to within close limits stoicheiometric compositions, and this would have been most unlikely if significant decomposition had occurred. Point (*b*) was eliminated by the fact that addition of acetone to the mother-liquors in the proportions used in the washing procedure gave no precipitates in the time interval required to complete the washing. For these reasons, the compositions assigned to the solid phases in Tables 3, 4, and 5 are believed correct. The nature of the three phases D, E, and "acidic" anhydrous $Al_2(SO_4)_3$, whose compositions were not truly stoicheiometric, will be discussed below.

Further confirmation of the acidic nature of the solid phases was obtained by comparison of the *X*-ray powder photographs of corresponding aluminium and ferric compounds. In making these and subsequent comparisons, it was essential to compare the actual photographic films and not sets of calculated lattice spacings, for with the latter, important similarities and differences could be overlooked. In the case of the 1,1,8 compounds, the photographs were practically identical, showing that the two solids were isomorphous and therefore had the same atomic composition. For the 1,1,2 and anhydrous pairs of compounds, the photographs were sufficiently similar to indicate distinct possibilities of isomorphism. It is noteworthy that the characteristic features of the photographs of the 1,1,2 pair were also found in $(NH_4)_2SO_4,Fe_2(SO_4)_3$, showing that the oxonium ion may be replaced isomorphously by the ammonium ion (cf. Shiskin, *Zhur. Obs. Khim.*, 1951, **21**, 456; *Chem. Abs.*, 1951, **45**, 6115). Lattice dimensions and space-groups already known for $K_2SO_4,Al_2(SO_4)_3$, $(NH_4)_2SO_4,Al_2(SO_4)_3$, and $(NH_4)_2SO_4,Fe_2(SO_4)_3$ ("Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., 31st edn., 1949, p. 2056, 2062) show that these also are isomorphous and belong to the hexagonal class as does the aluminium 1,1,2 compound. This is convincing evidence that the last compound (*a*) has the composition denoted by 1,1,2, (*b*) is an oxonium salt, and (*c*) is not the dihydrate of the normal sulphate. The *X*-ray diagram of $(NH_4)_2SO_4,Fe_2(SO_4)_3,4H_2O$ showed no resemblance to any of the other compounds dealt with in this paper.

In the case of coquimbite and the 9-hydrate of aluminium sulphate, less resemblance could be traced between the photographs than was expected, for it is well known that up to 50% of the iron in coquimbite can be replaced by aluminium. The lack of resemblance may cast doubt on the nature of the aluminium compound, but on the other hand it is known that coquimbite, and probably therefore the corresponding aluminium compound also, is polymorphous, and since the aluminium compound was prepared at 160°, the photographs may be those of structurally unrelated polymorphs.

The determination of numerous invariant points, either directly or by extrapolation of solubility curves (Table 3), allowed the direction of the univariant lines for the transitions 16-hydrate $\longrightarrow$ 1,1,12, 16-hydrate $\longrightarrow$ 2,1,24, and 1,1,12 $\longrightarrow$ 1,1,8 to be fixed on the polythermal projection diagram with certainty, so the empirical criteria suggested by Taylor (*loc. cit.*) for distinguishing between normal and acid sulphates could be applied. According to these criteria, for the first two transitions where an increase in acid content occurs in the direction from left to right, points on the univariant lines would be expected to show an increase in sulphuric acid concentration with rising temperature, while for the third transition, where dehydration occurs from left to right, an increase in water concentration could be expected. It should be noted that the first two transitions also involve dehydration from left to right, and depending on whether the hydrate or acid sulphate characteristics of the phases on the right-hand side are predominant, the direction of the univariant lines may follow either the water of the acid criteria respectively. In fact, all three transitions do conform to the hydrate–lower hydrate case, and it may therefore be that the hydrate nature of the phases is the more important, a view which is not unreasonable in view of their high degree of hydration. Owing to very stubborn metastability, invariant points and

univariant lines for the transitions 16-hydrate ⟶ 14-hydrate, 14-hydrate ⟶ 2,1,24, and 2,1,24 ⟶ 1,1,12 were obtained only by considerable extrapolation of solubility curves and are therefore less reliable. Nevertheless, Fig. 2 suggests that the first transition does conform to the hydrate–lower hydrate case, and the second and third to the hydrate–acid sulphate criterion. According to Posnjak and Merwin's data (*loc. cit.*), transitions which involve simultaneously dehydration and an increase in the acid content of the solid phases do not occur in the corresponding ferric sulphate system; all transitions conform without ambiguity to Taylor's criteria although the position is complicated by retrograde solubility.

The nature of the non-stoicheiometric solid phases can be considered as follows. Since the *X*-ray powder photograph of " acidic " anhydrous $Al_2(SO_4)_3$ was identical even in the high-order lines with that of the true anhydrous salt, the two must have the same lattice structure. Since the extra acid and water in the former were present in roughly the same proportions as in the mother-liquor and were shown to be contained within the crystals and not on the surface, the presence of inter-crystallite liquid is indicated. The relationship between the 1,1,2 and the " acidic " 1,1,2 phase is not so simple, for although the powder photographs showed that they were both essentially the same chemical individual, yet the absence from the " acidic " 1,1,2 photograph of two or three of the low-order lines of moderate intensity pointed to slight differences in lattice structure. The latter, it is suggested, may be the result of lattice defects caused by the occasional absence of an aluminium ion, electrical neutrality being preserved by the substitution of three hydrogen ions in its place. The " holes " would be distributed on a statistical basis and the hydrogen ions would be associated with oxygen atoms of SO_4^{--} ions. Such a substitution process would be analogous to that known to occur in the alunite series (Bassett and Goodwin, *loc. cit.*), and would result in the " acidic " phase's varying slightly in composition from one preparation to another, as was in fact observed. The substitution on the average of one aluminium ion in every 16 transforms the composition 1,1,2 into 1,1·27,2·14 which would account very well for the acid concentration of the " acidic " phase. The latter's water content however varied between 2·46 and 3·68 molecules, which suggests that inclusion of acidic liquid had occurred in addition to a degree of substitution less than one in 16. Considering the habit of the " acidic " phase, inclusion of liquid would be very probable. Since the points representing the dry solid lay significantly on the water side of the corresponding group of tie-lines, absorption of a small quantity of liquid richer in water than the mother-liquor may have occurred during the washing procedure. Comparison of powder photographs showed that other transformations such as 9-hydrate ⟶ 1,1,12 and 6-hydrate ⟶ 1,1,8, caused by the substitution of one aluminium ion in every four, had not occurred. In view of the composition, tie-line and indicator experiment data for the metastable phase D, the latter is best regarded as a second form of the 1,1,8 compound. The *X*-ray data showed that the structures of the two forms were probably unrelated, and the extra sulphuric acid in the metastable form may therefore arise from occluded liquid.

The divergence of opinion of previous authors regarding the nature of the solid phases is probably due to the two factors: (*a*) too great reliance being placed on apparent tie-line convergence and (*b*) the existence of metastable equilibria. For example, it would be difficult on the basis of tie-line data alone to distinguish with certainty between the solid phases 1,1,8, 1,2,10, and 1,3,12, and although Henry and King (*loc. cit.*) have reported the solid 1,3,12, their description of the phase corresponds almost exactly with the stable form of our 1,1,8 substance. Similar difficulties apply to the two trios 9-hydrate–1,1,12–2,1,24 and anhydrous–dihydrate–1,1,2. Henry and King also report at 60°, following the acidic 1,3,12 (or more probably 1,1,8) with increasing acid concentration, the surprising appearance of the anhydrous normal sulphate. This phase may, as mentioned above, have been mistaken for the 1,1,2 compound, or their solutions may have been metastable with respect to 1,1,2, for we have observed the " acidic " anhydrous phase (prepared separately) to persist with the " acidic " 1,1,2 phase in contact with saturated solution (*ca.* 80% of free acid) for twelve months at 25—60° without showing any signs of approach to true equilibrium. On the other hand, we have never observed the formation of the " acidic " anhydrous phase in solution below about 200°.

Appendix

The *X*-ray photographs were taken with a 9-cm. camera, Cu-*K*α radiation being used for the aluminium compounds, and Co-*K*α for the ferric compounds. Only the first 10—15 lines are recorded, though many more were visible in different cases. Intensities were estimated visually; s signifies strong, m moderate, w weak. In Table 7, the spacings *d* are given in Ångström units. The spacings for $Fe_2(SO_4)_3,H_2SO_4,8H_2O$ agree with, but are more complete than, those given by Amiel, Gourdonneau, and Vauthier (*Compt. rend.*, 1945, **220**, 402). Their results for $Fe_2(SO_4)_3,9H_2O$, prepared by Recoura's method (*Ann. Chim. Phys.*, 1907, **11**, 264), differ appreciably from those given below for $Al_2(SO_4)_3,9H_2O$ or coquimbite.

Table 7. *Lattice spacings.*

$Al_2(SO_4)_3,14H_2O$		$Al_2(SO_4)_3,9H_2O$		$Al_2(SO_4)_3,6H_2O$		$Al_2(SO_4)_3$		Alunite		Al, 1,1,12	
d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
7·37	w	7·56	m	7·74	w	5·72	m	4·95	m	8·28	w
5·62	w	5·50	w	6·70	m	4·19	m	3·57	w	7·40	w
5·15	w	4·64	s	5·58	w	3·47	s	3·01	s	6·12	w
4·55	s	4·26	s	4·73	s	2·88	m	2·79	w	4·74	m
4·26	m	3·80	s	4·03	w	2·63	m	2·25	m	4·32	s
3·91	m	3·48	s	3·80	m	2·58	m	1·91	m	4·08	m
3·63	m	3·14	m	3·59	m	2·33	w	1·87	w	3·86	w
3·29	w	2·98	m	3·29	m	2·29	w	1·75	m	3·68	m
2·98	w	2·71	m	3·01	m	2·19	m	1·65	w	3·55	w
2·78	w	2·64	w	2·67	w	2·02	m	1·55	w	3·27	w
2·66	w					1·98	w	1·48	w	3·14	w
2·59	w					1·92	m	1·46	m	2·99	m
2·53	w									2·80	m
										2·66	w
										2·56	m

Al, 1,1,8, stable		Al, 1,1,8, metastable		Al, "acidic," 1,1,2		Al, 1,1,2		Coquimbite		$Fe_2(SO_4)_3,8H_2O$	
d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
9·40	s	6·27	w	8·28	m	10·48	s	9·63	w	10·54	m
8·96	s	5·19	w	4·06	m	7·82	m	8·58	s	7·23	w
5·12	w	4·68	s	3·93	m	4·04	w	5·53	m	6·87	s
4·68	s	4·16	w	3·74	w	3·86	m	4·65	m	5·26	w
4·40	w	3·97	w	3·40	s	3·70	m	3·64	m	4·84	w
3·99	m	3·89	w	3·14	w	3·57	m	3·49	w	4·45	m
3·65	w	3·74	m	2·90	w	3·34	s	3·36	m	4·22	w
3·46	m	3·61	m	2·64	m	3·09	w	3·03	w	4·01	w
3·26	m	3·48	m	2·37	m	2·95	w	2·77	s	3·58	m
3·04	s	3·14	w	2·26	m	2·85	w	2·54	w	3·35	w
2·69	w	2·99	w	2·03	w	2·73	w	2·31	w	3·22	w
2·66	w	2·89	w	1·94	w	2·58	m				
2·59	w	2·80	w			2·35	m				
2·56	w	2·76	w			2·31	w				
2·49	w	2·61	w			2·26	m				

Fe, 1,1,8		Fe, 1,1,2		$Fe_2(SO_4)_3$		$(NH_4)_2SO_4,Fe_2(SO_4)_3$		$(NH_4)_2SO_4,Fe_2(SO_4)_3,4H_2O$	
d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
9·22	s	10·28	m	6·08	m	8·10	s	6·91	w
8·81	s	9·01	m	5·32	w	4·49	w	5·77	s
5·19	w	7·72	m	4·40	m	4·10	w	5·15	w
4·79	w	4·05	w	4·14	m	3·67	w	4·55	w
4·68	m	3·90	w	3·71	w	3·41	m	3·80	s
4·18	w	3·71	w	3·59	s	2·69	w	3·27	s
4·01	m	3·59	w	3·26	w	2·39	m	2·88	w
3·50	m	3·35	s	3·16	w	2·07	w	2·77	w
3·26	m	3·26	w	2·99	m	1·96	w	2·67	w
3·08	m	3·08	w	2·90	w				
2·75	w	2·57	w	2·74	m				
2·64	w	2·39	m	2·69	w				
2·57	w	2·27	w	2·63	w				
2·49	w	2·02	w	2·42	w				

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University of Edinburgh.

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851. *The Preparation of Some Alkyl-substituted Benzoic Acids.*

By MALCOLM CRAWFORD and F. H. C. STEWART.

Improved general routes have been employed for the preparation of *o*- and *m*-alkylbenzoic acids applicable to primary, *sec.*-, and *tert.*-alkyl groups. The corresponding *o*- and *m*-alkylbromobenzenes are intermediates. Routes for the preparation of some 2 : 4 : 6-tri- and 2 : 3 : 4 : 6-tetra-substituted benzoic acids are also described.

DURING work which will be described in a later paper, it became necessary to prepare a number of alkyl-substituted benzoic acids. Although it is possible to obtain *p*-alkylbenzoic acids without difficulty, the methods available for *o*- and *m*-acids are mainly unsatisfactory : awkward separations of isomers are frequently involved, yields are poor, and the routes employed are often applicable only to particular alkyl groups. The Clemmensen reduction of aryl alkyl ketones, for example, can only give primary alkyl groups from ethyl upwards. The reduction of phthalides, substituted or unsubstituted, which has commonly been used for *o*-acids, is tedious and of limited application. Hence it was found necessary to devise new routes or to apply existing routes by suitable modification to the syntheses of the acids required.

The improved route A1 for *sec.*- and *tert.*- and the new route A2 for primary alkylbromobenzenes and benzoic acids have proved satisfactory when using Pr^i, Bu^t, and Et respectively. Shoesmith and Mackie (*J.*, 1928, 2339) have already used route A1 for *o-tert.*-butylbenzoic acid (V; R = Bu^t) but the bromination stage is difficult and erratic. In Derbyshire and Waters's bromination method (*J.*, 1950, 573) difficulties vanish and high yields are obtained. The deamination stage has also been improved by using hypophosphorous acid as the reducing agent, and better yields are obtained in the carboxylation of the Grignard reagent by using solid carbon dioxide. This route also gives a good yield of *o-iso*propylbenzoic acid (V; R = Pr^i) previously obtained by reduction of 3 : 3-dimethylphthalide with hydriodic acid and phosphorus in a sealed tube (Kothe, *Annalen*, 1888, **248**, 63).

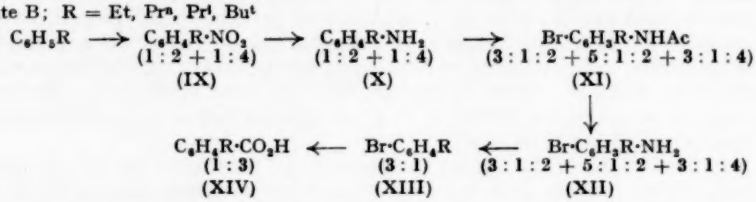
* Route A1; R = Pr^i, Bu^t

$$C_6H_5 \longrightarrow \underset{(1:4)}{C_6H_4R{\cdot}NO_2} \longrightarrow \underset{(2:1:4)}{Br{\cdot}C_6H_3R{\cdot}NO_2} \longrightarrow \underset{(2:1:4)}{Br{\cdot}C_6H_3R{\cdot}NH_2} \longrightarrow \underset{(2:1)}{Br{\cdot}C_6H_4R} \longrightarrow \underset{(1:2)}{C_6H_4R{\cdot}CO_2H}$$
$$\qquad\qquad\qquad

up the position, coplanar with the ring, which is necessary for the deactivation. Neither the nitro-acid nor its ethyl ester can be brominated or nitrated, an observation which indicates the reluctance of groups to enter the 6-position next to a *tert.*-butyl group when the 2-position is already occupied. This point is dealt with elsewhere (Crawford and Stewart, *Nature*, 1952, **170**, 322).

Route B has proved very satisfactory for the preparation of *m*-alkyl-substituted benzoic acids and is based on methods used for the preparation of *o*- and *p*-ethylaniline (Cline and Reid, *J. Amer. Chem. Soc.*, 1927, **49**, 3150), *m*-bromocumene (Sterling and Bogert, *J. Org. Chem.*, 1939, **4**, 20), and *m*-bromo-*tert.*-butylbenzene (Gelzer, *Ber.*, 1888, **21**, 2944). There is no need to separate the *o*- and *p*-nitro-compounds (IX), or the corresponding amines (X), or the mixture of three bromoacetanilides (XI), or even the mixed amines (XII), for on deamination the same *m*-bromohydrocarbons (XIII) result from all three. Where R is a tertiary group the amount of *o*-intermediate obtained is so small that it is

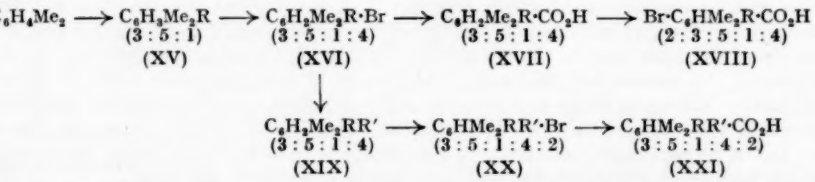
* Route B; R = Et, Pr^n, Pr^i, Bu^t


C6H5R
C6H4R·NO2 (1 : 2 + 1 : 4) (IX)
C6H4R·NH2 (1 : 2 + 1 : 4) (X)
Br·C6H3R·NHAc (3 : 1 : 2 + 5 : 1 : 2 + 3 : 1 : 4) (XI)
Br·C6H3R·NH2 (3 : 1 : 2 + 5 : 1 : 2 + 3 : 1 : 4) (XII)
Br·C6H4R (3 : 1) (XIII)
C6H4R·CO2H (1 : 3) (XIV)

eliminated in the recrystallisation of the bromoacetanilides, only the pure *p*-compound being recovered. It is interesting that *m-iso*propylbenzoic acid was found to melt at 47°, whereas Calcott, Tinker, and Weinmeyer (*J. Amer. Chem. Soc.*, 1939, **61**, 1010) reported m. p. *ca.* 20°. *m*-Propylbenzoic acid is a new compound, *m*-ethylbenzoic acid had only been prepared by lengthy methods from *m*-diethylbenzene (Voswinkel, *Ber.*, 1888, **21**, 2830) and from *m*-nitroacetophenone (Mayer and English, *Annalen*, 1918, **417**, 87), and *m-tert.*-butylbenzoic acid had been prepared by various routes from *m-tert.*-butyltoluene, in turn obtained along with the *p*-isomer from toluene (Kelbe and Pfeiffer, *Ber.*, 1886, **19**, 1725; Shoesmith and Mackie, *J.*, 1936, 300; Serijan, Hipscher, and Gibbons, *J. Amer. Chem. Soc.*, 1949, **71**, 873), but Shoesmith and Mackie do refer to its preparation from *m*-bromo-*tert.*-butylbenzene for purposes of orientation.

Methods are available for the preparation of dialkylbenzoic acids and a number of them are referred to in the following paper. To prepare certain tri- and tetra-alkylbenzoic acids, route C has been used. 2 : 4 : 6-Trimethylbenzoic (mesitoic) acid (XVII; R = Me) is generally prepared by two of the stages in this route since mesitylene is available (*Org. Synth.*, 1941, **21**, 77). The Friedel–Crafts method used by Nightingale and Smith (*J. Amer. Chem. Soc.*, 1939, **61**, 101) to obtain 1 : 3 : 5-*tert.*-butyl-*m*-xylene (XV; R = Bu^t) from *m*-xylene renders 4-*tert.*-butyl-2 : 6-dimethylbenzoic acid readily accessible. This acid was mistakenly described as the isomeric 2-*tert.*-butyl-4 : 6-dimethylbenzoic acid by Baur-Thurgau (*Ber.*, 1898, **31**, 1348), an error corrected by Tchitchibabine (*Bull. Soc. chim.*, 1932, **51**, 1436).

* Route C.


C6H4Me2
C6H3Me2R (3 : 5 : 1) (XV)
C6H2Me2R·Br (3 : 5 : 1 : 4) (XVI)
C6H2Me2R·CO2H (3 : 5 : 1 : 4) (XVII)
Br·C6HMe2R·CO2H (2 : 3 : 5 : 1 : 4) (XVIII)
C6H2Me2RR′ (3 : 5 : 1 : 4) (XIX)
C6HMe2RR′·Br (3 : 5 : 1 : 4 : 2) (XX)
C6HMe2RR′·CO2H (3 : 5 : 1 : 4 : 2) (XXI)

Bromination of (XVII; R = Bu^t) gives an almost quantitative yield of the mono-bromo-compound (XVIII). Little if any of the dibromo-compound appears to be formed even under the forced conditions used. This is further evidence of the resistance to

substitution in the *o*-position to a *tert.*-butyl group when the other *o*-position is occupied (Crawford and Stewart, *loc. cit.*).

The replacement of bromine in (XVI; R = Me) by ethyl through the action of diethyl sulphate on the Grignard reagent gives a 55% yield of ethylmesitylene (XIX; R = Me, R′ = Et). An attempt was made to prepare *tert.*-butylmesitylene (XIX; R = Me, R′ = Bu^t) by treating mesitylmagnesium bromide with *tert.*-butyl chloride, but the main product obtained was mesitylene. Once again the *tert.*-butyl group avoids the presence of two large *o*-substituents. 3-Ethyl-2 : 4 : 6-trimethylbenzoic acid (XXI; R = Me, R′ = Et) is interesting in that it has an abnormally high melting point compared with other ethyl-substituted acids. It is hoped to report on this in a later paper.

Experimental

Analyses, except for copper, are by Drs. Weiler and Strauss, Oxford. M. p.s are not corrected.

2-*Bromo*-4-*nitrocumene* (II; R = Pr^i).—*p*-Nitrocumene (33 g.), prepared by Sterling and Bogert's method (*loc. cit.*), silver sulphate (34 g.), concentrated sulphuric acid (180 ml.), and water (20 ml.) were stirred with gradual addition of bromine (10·4 ml.). Stirring was continued for 2 hours, and then the mixture was poured into dilute sodium hydrogen sulphite solution (1000 ml.). The oil which separated was taken up in ether, and the remaining aqueous liquid extracted with ether. The mixed ethereal solutions were dried and distilled, finally under reduced pressure. The 2-bromo-4-nitrocumene distilled at 155—160°/15 mm. as a yellow oily liquid (78%) which did not solidify at −20°.

3-*Bromo*-4-iso*propylaniline* (III; R = Pr^i).—2-Bromo-4-nitrocumene (40 g.) was reduced with iron and ethanolic hydrogen chloride. The resulting amine was a reddish-brown oil (80%), b. p. 150°/15 mm. Its *benzoyl* derivative crystallised from aqueous ethanol in needles, m. p. 151° (Found: C, 60·0; H, 5·1. $C_{16}H_{14}ONBr$ requires C, 60·4; H, 5·1%).

o-*Bromocumene* (IV; R = Pr^i).—3-Bromo-4-*iso*propylaniline (21·5 g.) was dissolved in concentrated hydrochloric acid (40 ml.), diluted with water (80 ml.), and poured on ice (100 g.). An aqueous solution of sodium nitrite (7 g. in 15 ml.) was added, and the filtered diazonium solution treated with 50% hypophosphorous acid (150 ml.) and kept in ice for 24 hours. The oil which separated was extracted with ether, the extract dried ($MgSO_4$), the ether distilled off, and the residue distilled under reduced pressure, leaving a colourless oil (60%), b. p. 90°/15 mm. Fileti (*Gazzetta*, 1886, **16**, 131) had prepared this substance by the action of phosphorus pentabromide on *m-iso*propylphenol.

o-iso*Propylbenzoic Acid* (V; R = Pr^i).—*o*-Bromocumene (12 g.) was converted into the Grignard reagent in the usual way and poured on an excess of powdered solid carbon dioxide. The syrupy product was treated with hydrochloric acid, the ethereal layer separated and extracted with dilute sodium hydroxide solution, and the extract acidified. The crude acid so obtained crystallised from light petroleum; the product (66%) had m. p. 54°.

2-*Bromo*-1-tert.-*butyl*-4-*nitrobenzene* (II; R = Bu^t).—Crude *p-tert.*-butylnitrobenzene (142 g.) containing some *o*-isomer was brominated by Derbyshire and Waters's method as described above. The product crystallised from ethanol in needles (80%), m. p. 94°.

o-*Bromo*-tert.-*butylbenzene* (IV; R = Bu^t).—The foregoing nitro-compound (134 g.) was reduced with iron and ethanolic hydrogen chloride. The amine separated as the hydrochloride (85%), a portion of which (57 g.) was diazotised and the product reduced with hypophosphorous acid. The resulting oil (75%) had b. p. 96—98°/12 mm. Another portion of the hydrochloride was diazotised and treated with alkaline formaldehyde according to Brewster and Poje's method (*J. Amer. Chem. Soc.*, 1939, **61**, 2418) but the yield of *o*-bromo-*tert.*-butylbenzene was only 7%.

o-tert.-*Butylbenzoic acid* (V; R = Bu^t).—*o*-Bromo-*tert.*-butylbenzene (20 g.) was converted into the Grignard reagent and treated with solid carbon dioxide. The acid was recrystallised from light petroleum, and then had m. p. 68·5° (yield 60%). Serijan, Hipscher, and Gibbons (*loc. cit.*) give m. p. 80·8° (corr.).

2-tert.-*Butyl*-5-*nitrobenzoic Acid* (VI; R = Bu^t).—*o-tert.*-Butylbenzoic acid (10 g.) was heated with nitric acid (*d* 1·42; 25 ml.) on the water-bath for 2½ hours. The *nitro-acid*, obtained by pouring the mixture on ice, crystallised from benzene in needles (79%), m. p. 170° (Found: C, 59·8; H, 6·0; N, 6·3. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·9; N, 6·3%). Attempts to brominate and nitrate this acid by heating it with bromine and nitric acid, respectively, failed. Only the starting material was recovered from the reaction mixture.

Ethyl 2-tert.-*Butyl-5-nitrobenzoate*.—The silver salt obtained from the free acid (5 g.) on treatment with ethyl iodide gave the ethyl ester as a yellow oil (84%), b. p. 190°/15 mm. Attempts to brominate and nitrate this ester similarly to the acid failed.

Copper 2-tert.-*Butyl-5-nitrobenzoate*.—Addition of excess of copper sulphate solution to a neutralised solution of the acid threw down a precipitate which was filtered off, washed, and dried. Extraction with hot benzene–ethanol gave a dark green *copper* salt (Found: Cu, 13·2. $C_{22}H_{24}O_8N_2Cu$ requires Cu, 13·1%). The insoluble residual light greenish-blue material appeared to be a basic *salt* (Found: Cu, 23·0. $C_{11}H_{13}O_5NCu$ requires Cu, 21·8%).

1-*Bromo-2-ethyl-3* : 5-*dinitrobenzene* (VII; R = Et).—2 : 4-Dinitroethylbenzene (60 g.), prepared from ethylbenzene according to Brady, Day, and Allam (*J.*, 1928, 980), was brominated by Derbyshire and Waters's method except that all the bromine was added at once out of direct sunlight. 1-*Bromo-2-ethyl-3* : 5-*dinitrobenzene* was isolated as a golden-yellow oil, b. p. 180°/12 mm., which solidified in the cold to yellow crystals (80%), m. p. 25° (Found: C, 36·7; H, 2·7; N, 11·2. $C_8H_7O_4N_2Br$ requires C, 34·9; H, 2·6; N, 10·2%).

3 : 5-*Diamino*-1-*bromo*-2-*ethylbenzene* (VIII; R = Et).—1-Bromo-2-ethyl-3 : 5-dinitrobenzene (35 g.) was reduced with iron and ethanolic hydrogen chloride. The *diamine* was obtained as orange-brown crystals (74%) (from aqueous ethanol), m. p. 88° (Found: C, 44·7; H, 5·2; N, 13·2. $C_8H_{11}N_2Br$ requires C, 44·7; H, 5·2; N, 13·0%).

o-*Bromoethylbenzene* (IV; R = Et).—The foregoing diamine (20 g.) was diazotised and reduced with hypophosphorous acid. A large amount of tar was formed. The *o*-bromoethylbenzene had b. p. 85—90°/15 mm. (yield, 15%).

o-*Ethylbenzoic Acid* (V; R = Et).—*o*-Bromoethylbenzene (2·4 g.) was converted into the Grignard reagent and carboxylated with solid carbon dioxide. The acid (64%), crystallised from hot water, had m. p. 65°.

m-*Bromoethylbenzene* (XIII; R = Et).—Nitration of ethylbenzene (60 g.) according to Cline and Reid's method (*loc. cit.*) gave a mixture of *o*- and *p*-nitroethylbenzene (91%), which was reduced to give mixed *o*- and *p*-ethylaniline (75%). Acetylation followed by bromination afforded a mixture of three bromoacetanilides (81%). Hydrolysis of this gave the mixed bromoethylanilines (93%). m-*Bromoethylbenzene* was formed on deamination of the mixed amines by diazotisation and treatment with hypophosphorous acid; the bromo-compound (62%) had b. p. 96°/15 mm. (Found: C, 53·0; H, 5·0; Br, 42·2. C_8H_9Br requires C, 51·9; H, 4·9; Br, 43·2%); it did not possess the penetrating peppermint odour of the *o*- and *p*-isomers.

m-*Ethylbenzoic Acid* (XIV; R = Et).—*m*-Bromoethylbenzene (20 g.) was converted, by carboxylation of the Grignard reagent, into the acid (71%), long needles, m. p. 45°.

m-*Bromopropylbenzene* (XIII; R = Pr^n).—*n*-Propylbenzene (30 g.) was nitrated according to Brady and Cunningham's method (*J.*, 1934, 123) to give mixed *o*- and *p*-nitropropylbenzene (71%), which were reduced to the mixed amines (74%). These in turn were acetylated and brominated, giving the mixed bromopropylacetanilides (86%). Hydrolysis then gave the mixed bromopropylaniline hydrochlorides (91%), which were deaminated to *m*-bromopropylbenzene (65%), b. p. 100°/15 mm.

m-*Propylbenzoic Acid* (XIV; R = Pr^n).—*m*-Bromopropylbenzene (7 g.) was converted by carboxylation of the Grignard reagent into m-*propylbenzoic acid* (56%), m. p. 43° (from aqueous ethanol) (Found: C, 73·0; H, 7·3. $C_{10}H_{12}O_2$ requires C, 73·1; H, 7·4%).

p-*Aminocumene* (X; R = Pr^i).—*p*-Nitrocumene (65 g.), prepared by nitration of cumene, was reduced with tin and hydrochloric acid, giving the amine (75%) as a colourless oil, b. p. 115°/15 mm., probably containing some *o*-isomer. Sterling and Bogert (*loc. cit.*) refer to it as a golden-brown oil.

m-iso*Propylbenzoic Acid* (XIV; R = Pr^i).—*p*-Aminocumene (41·5 g.) was acetylated and brominated to give 2-bromo-4-*iso*propylacetanilide (m. p. 131°, after recrystallisation). The bulk was hydrolysed to 4-amino-3-bromocumene (87% yield on *p*-aminocumene), a reddish-brown oil, b. p. 140—145/15 mm., which was deaminated to *m*-bromocumene (67%), a colourless liquid, b. p. 90—95°/15 mm., which was converted into the acid by carboxylation of the Grignard reagent; the acid (69%) had m. p. 47—48° (from light petroleum) (Found: C, 72·6; H, 7·1. Calc. for $C_{10}H_{12}O_2$: C, 73·1; H, 7·4%).

p-tert.-*Butylacetanilide*.—*p-tert.*-Butylnitrobenzene (80 g.), prepared by nitration of *tert.*-butylbenzene and containing some *o*-isomer, was reduced by Craig's method (*J. Amer. Chem. Soc.*, 1935, **57**, 195). A brown solid which separated was removed (see below). The crude amine was acetylated, and the product recrystallised twice from aqueous ethanol, then having m. p. 176° (yield, 51%). This was obviously the pure *p*-isomer.

4 : 4′-*Di*-tert.-*butylazobenzene*.—The brown solid from the previous preparation, on recrystal-

lisation from ethanol, gave reddish-brown needles, m. p. 185° (Malherbe, *Ber.*, 1919, **52**, 323, gives m. p. 183°) (Found : C, 81·2; H, 8·9; N, 9·7. Calc. for $C_{20}H_{26}N_2$: C, 81·6; H, 8·9; N, 9·5%).

m-tert.-*Butylbenzoic Acid* (XIV; R = Bu^t).—*p-tert.*-Butylacetanilide (10 g.) was brominated to the 3-bromo-compound (XI; R = Bu^t) which, recrystallised from benzene, had m. p. 138·5° (85%). This was hydrolysed to the amine (90%), b. p. 140°/15 mm. This in turn was deaminated to *m*-bromo-*tert.*-butylbenzene (70%), b. p. 100°/40 mm. Carbonation of the Grignard reagent then gave *m-tert.*-butylbenzoic acid which, recrystallised from light petroleum, had m. p. 127° (60%).

2-*Bromo*-5-tert.-*butyl*-m-*xylene* (XVI; R = Bu^t).—1-*tert.*-Butyl-*m*-xylene (70 g.), prepared by Nightingale and Smith's method (*loc. cit.*), was cooled in ice and treated with iodine (0·5 g.) followed by bromine (23·5 ml.) added during 2 hours. Next morning, the mixture was washed with warm sodium hydroxide solution and then warm water. The oily layer was separated, dried, and distilled. Redistillation gave the substituted *m*-xylene (81%), b. p. 140°/15 mm., m. p. 45°. Tchitchibabine (*loc. cit.*) prepared this substance by an indirect method from the following acid.

4-tert.-*Butyl*-2 : 6-*dimethylbenzoic Acid* (XVII; R = Bu^t).—2-Bromo-5-*tert.*-butyl-1 : 3-dimethylbenzene (20 g.) was converted into the acid by carboxylation of the Grignard reagent; recrystallised from petroleum (b. p. 100—120°), it (68%) had m. p. 168°.

3-*Bromo*-4-tert.-*butyl*-2 : 6-*dimethylbenzoic Acid* (XVIII; R = Bu^t).—The foregoing acid (1 g.) was treated with a crystal of iodine followed by bromine (0·5 ml.) added during a short period at room temperature. Hydrogen bromide was evolved and there resulted a practically quantitative yield of the *bromo-acid*, needles [from petroleum (b. p. 100—120°)], m. p. 169° (Found : C, 53·9; H, 6·2. $C_{13}H_{17}O_2Br$ requires C, 54·7; H, 6·0%). The acid remained unchanged even when boiled with bromine.

Ethylmesitylene (XIX; R = Me, R′ = Et).—Prepared by treating the Grignard reagent formed from bromomesitylene (30 g.) with ethyl sulphate (100 ml.), this had b. p. 214° (60%).

2-*Bromo*-6-*ethylmesitylene* (XX; R = Me, R′ = Et).—Ethylmesitylene (5·8 g.) in glacial acetic acid (10 ml.) was treated with iodine (one crystal) and bromine (2·2 ml.) in glacial acetic acid (6·2 ml.). The mixture was poured into a cooled dilute solution of sodium hydrogen sulphite and extracted with ether, and the extract dried and distilled. The product (74%) had b. p. 135—140°/15 mm.

3-*Ethyl*-2 : 4 : 6-*trimethylbenzoic Acid* (XXI; R = Me, R′ = Et).—Bromoethylmesitylene (5 g.) was converted into the acid by carboxylation of the Grignard reagent. The *acid* (64%) was obtained as micro-crystals, m. p. 143° (Found : C, 74·0; H, 8·3. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%).

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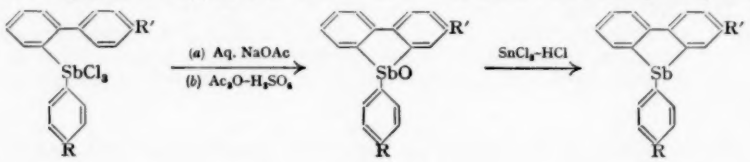
852. *The Configuration of Heterocyclic Antimony Compounds. Part II.* Symmetric and Enantiomorphic 9-Stibiafluorenes.*

By I. G. M. Campbell.

Fractional crystallisation of optically active base salts of 9-*p*-carboxyphenyl-9-stibiafluorene gives no evidence of the existence of diastereoisomerides. On the other hand, 2-amino-9-*p*-tolyl-9-stibiafluorene is resolved into (+)- and (−)-forms by crystallisation of the (+)- and (−)-hydrogen tartrates, and the enantiomers, $[\alpha]_D^{22}$ ±250°, show considerable optical stability. A study of the racemisation of the (+)-base in benzene at 22°, 25·4°, 30°, and 40° indicates that the energy of activation is about 15 kcal./mole, but since the racemisation appears to be subject to adventitious catalysis, this figure is quoted with reservation. The successful optical resolution of the (±)-base, and the failure of all attempts to resolve the stibiafluorene unsubstituted in the diphenyl residue, constitute further evidence that enantiomorphism of this type of heterocyclic compound is dependent on the stable pyramidal disposition of the valency bonds of the tervalent antimony atom and not on the "skew" configuration of the diphenyl residue in the molecule.

In Part I * the preparation and properties of (+)- and (−)-2-carboxy-9-*p*-tolyl-9-stibiafluorene (III; R = Me, R′ = CO_2H) were described, and the reasons for the choice of the 9-stibiafluorenes as a molecular type suitable for investigating the stereochemistry of antimony were discussed. Unfortunately, the discovered asymmetry could not be ascribed with certainty to the stable pyramidal disposition of the bonds of the tervalent antimony atom because the possible twisting of the benzene rings in the tricylic system could deprive the molecule of any symmetry even if the bonds from antimony were planar. However, if the distortion of this part of the molecule to accommodate the antimony atom is the cause of the enantiomorphism, a symmetrically substituted 9-stibiafluorene [*e.g.*, (III; R = CO_2H, R′ = H)] should be a "skew" molecule and consequently should be



resolvable into (+)- and (−)-forms. To test this hypothesis, 9-*p*-carboxyphenyl-9-stibiafluorene was prepared by a method essentially that described in Part I (*loc. cit.*), and optical resolution was attempted. The acid formed unsatisfactory salts with brucine and quinidine but fractional crystallisation of the salts obtained with quinine, ephedrine, and (+)-1-phenylethylamine gave no evidence of separation into diastereoisomerides, and acid regained from the salts was consistently optically inactive. In contrast, 2-amino-9-*p*-tolyl-9-stibiafluorene, which should be dissymmetric if the bonds from antimony are not planar and the tricyclic system remains flat, was found to be readily resolvable through the (+)- and (−)-hydrogen tartrates and gave specimens of the (+)-amine, $[\alpha]_D^{22}$ +250·5°±1°, and (−)-amine, $[\alpha]_D^{23}$ −248·0°±2°, in benzene. Despite the fact that non-resolution of the symmetrically substituted acid constitutes negative evidence of an unsatisfactory kind, the striking contrast between the comparatively ready separation of (+)- and (−)-forms of both the unsymmetrically substituted stibiafluorenes so far investigated, and the homogeneity of the three salts of the unsubstituted compound, are an argument in favour of the pyramidal rather than the skew configuration of the molecule.

The resolution of the (±)-amine by use of (+)-tartaric acid was carried out by orthodox

* Part I, *J.*, 1950, 3109. The nomenclature of organic antimony acids in Part I was that recorded in A. D. Mitchell's "British Chemical Nomenclature," Ed. Arnold & Co., London, 1948, p. 64. In the present paper (Part II), however, it is based on that laid down in *J.*, 1951, 3516; *e.g.*, $Ph{\cdot}SbO_3H_2$ = phenylstibonic acid; Ph_2SbO_2H = diphenylstibinic acid.

procedures and no difficulty was experienced in the purification of the less soluble diastereoisomeride, (+)-acid (+)-base, m. p. 161—162° (decomp.), $[\alpha]_D$ +216·5°, provided that the ethanol used for crystallisation contained 2% of (+)-tartaric acid, otherwise the salt which separated was contaminated with free base. The more soluble (+)-acid (−)-base salt was never obtained optically pure and invariably separated as a gel, a tiresome characteristic which was mainly responsible for the low yields of optically pure base obtained. Moreover, the usual tendency for aromatic amine salts to develop colour in air was very marked in the case of the more soluble salt. As purification by crystallisation, either of the gelatinous (+)-acid (−)-base salt, or of the optically impure base regained from it, was unsuccessful, (−)-tartaric acid was used to obtain the (−)-acid (−)-base salt, m. p. 160—161° (decomp.), $[\alpha]_D$ −212·8°. [The discrepancy in the specific rotations of the enantiomeric salts arose from racemic acid present in the (−)-tartaric acid used.] As initial experiments indicated that racemisation was appreciable on warming, the (+)- and the (−)-amine were isolated by addition of 0·5N-sodium hydroxide to ethanolic solutions of the salts at −10° and immediate filtration of the crystalline base precipitated. The (+)-amine, $[\alpha]_D^{22}$ 250·5°, could not be recrystallised without some loss of optical activity.

The racemisation, in benzene, of one particular batch of the (+)-base was followed at 22°, 25·4°, 30°, and 40° and the rate constants were found to be 1·15, 1·61, 2·02, and $5{\cdot}16 \times 10^{-2}$ hour^{-1}, respectively. From these constants a linear Arrhenius plot resulted (the value of k_{30} was slightly low), leading to an energy of activation of 15 kcal./mole. However, the racemisation rate of the (−)-base at 22° was not identical with that of the (+)-base at the same temperature and the results obtained with the (+)-base at 30° were not reproducible, although the specimen used for the second experiment was obtained from the same salt and in the same way. Furthermore, on one occasion a portion of base, α_D^{20} +1·58°, $[\alpha]_D^{20}$ +248·4°, remained unchanged in rotation after a day, and after 3 weeks still had α_D +1·14°, $[\alpha]_D$ +179·2°. Obviously the racemisation is very susceptible to traces of adventitious catalyst, a not uncommon phenomenon observed for example in the racemisation of bromosuccinic ester by bromide ion in a concentration not detected analytically (R. Kuhn and T. Wagner-Juaregg, *Naturwiss.*, 1929, **17**, 103). In the present case the nature of the catalyst is obscure, although hydrochloric acid proved to be effective, for a specimen of optically impure (−)-base, α_D^{22} −0·80°, which had remained unchanged in rotation for 3 days, was " touched off " by introducing a trace of the vapour into the polarimeter tube. Racemisation started immediately and the rotation had fallen to zero within 2 days. Also, there occurred a very rapid racemisation, similar to that observed in the original attempts to isolate (+)-2-carboxy-9-*p*-tolyl-9-stibiafluorene (*J.*, 1950, 3111), when a chloroform solution of the (+)-base, α_D^{24} +1·20°, was shaken with 4N-hydrochloric acid. Neither the chloroform solution nor the acid showed any optical activity on polarimetric examination 20 minutes after mixing.

As the racemisation of (+)-2-carboxy-9-*p*-tolyl-9-stibiafluorene in pyridine at 40° was considerably slower than that of the (+)-amine in benzene at the same temperature, the possibility that pyridine was effective in stabilising the asymmetric molecule was investigated, but the (+)-base was found to racemise more rather than less rapidly in the basic solvent.

In view of these results it is clear that a much more detailed study of the racemisation is necessary in order to gain a precise value for the energy of activation, a value of considerable interest if the projected *X*-ray crystallographic examination indicates that the configuration of the stibiafluorenes is, in fact, pyramidal. 2-Amino-9-*p*-tolyl-9-stibiafluorene, a primary aromatic amine, slightly sensitive to light and air, is not an ideal subject for such a study, and the synthesis of further members of the series may disclose a compound more suitable for the purpose.

Experimental

Carbon and hydrogen analyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

p-*Carbethoxyphenyl*-2-*diphenylylstibine Trichloride* (I; R = CO_2Et, R′ = H).—This compound was prepared by the method described previously (*J.*, 1950, 3014) for 2-diphenylyl-*p*-

tolylstibine trichloride. 2-Aminodiphenyl (33·8 g., 0·2 mol.) was diazotised and converted into the antimony chloride double salt, which was isolated, washed with ethanol, and added in portions to *p*-carbethoxyphenylstibonous chloride (68·0 g., 0·2 mol.) in 125 c.c. of ethanol, 75 c.c. of which had been saturated with dry hydrogen chloride. Before all the double salt had been added, the trichloride began to crystallise out. The reaction was completed by warming to 40°, and the product was separated after cooling to 0°. Recrystallisation from ethyl acetate necessitated filtration from insoluble material (2 g.) and yielded the required *trichloride* (21 g., 20%), m. p. 144—146° (Found: C, 47·7; H, 3·7; Sb, 23·0. $C_{21}H_{18}O_2Cl_3Sb$ requires C, 47·5; H, 3·4; Sb, 22·95%). Reduction of the trichloride (1·3 g.) in ethanol (20 c.c.) with stannous chloride (1·5 g.) in 3N-hydrochloric acid (20 c.c.) gave, almost immediately, a crystalline precipitate of p-*carbethoxyphenyl*-2-*diphenylylstibinous chloride*, m. p. 84—85° (0·8 g.) (Found: C, 55·1; H, 4·4; Sb, 26·6. $C_{21}H_{18}O_2ClSb$ requires C, 54·9; H, 3·95; Sb, 26·5%).

9-p-*Carbethoxyphenyl*-9-*stibiafluorene* (III; R = CO_2Et, R′ = H).—The stibinic acid obtained by adding a solution of (I; R = CO_2Et, R′ = H) (11 g.) in acetone (150 c.c.) to aqueous sodium acetate was thoroughly dried and dissolved in acetic anhydride (100 c.c.) containing concentrated sulphuric acid (1 c.c.) and kept at 90° for 3 hours, then poured on ice and set aside overnight. The solid obtained was only partly soluble in acetone (50 c.c.), and the residue (5·2 g.) on recrystallisation from ethyl acetate proved to be 9-p-*carbethoxyphenyl*-9-*stibiafluorene oxide* (II; R = CO_2Et, R′ = H), m. p. 172—173° (decomp.) (Found: C, 57·4; H, 4·0. $C_{21}H_{17}O_3Sb$ requires C, 57·2; H, 3·9%). This oxide dissolved in acetone (40 c.c.) containing 3N-hydrochloric acid (10 c.c.) and was reduced with stannous chloride (5 g.), yielding 9-p-*carbethoxyphenyl*-9-*stibiafluorene*, m. p. 144—145° (4 g.) (Found: C, 59·9; H, 4·05; Sb, 28·9. $C_{21}H_{17}O_2Sb$ requires C, 59·6; H, 4·05; Sb, 28·8%). On reduction of the filtrate from the separation of the oxide, a further small quantity (0·7 g.) of the cyclic ester was obtained, but the main product was the stibinous chloride, m. p. 84—85° (3·3 g.).

The ester (7·5 g.) was hydrolysed by boiling for ½ hour in ethanol (150 c.c.) and 10% aqueous potassium hydroxide (70 c.c.). The reaction mixture was poured into water (300 c.c.) and acidified (Congo-red) with concentrated hydrochloric acid. Recrystallisation of the dry precipitate from ethanol–chloroform (1 : 1) gave 9-p-*carboxyphenyl*-9-*stibiafluorene* as small needles, m. p. 231—233° (Found: C, 57·7; H, 3·2; Sb, 30·9. $C_{19}H_{13}O_2Sb$ requires C, 57·75; H, 3·3; Sb, 30·8%).

Salts of 9-p-*Carboxyphenyl*-9-*stibiafluorene with Optically Active Bases.*—(+)-α-*Phenylethylamine salt.* This was prepared from the acid (1·6 g.) and twice the calculated quantity of (+)-base (1·0 g.) in ethanol–chloroform (1 : 1) (350 c.c.). The salt was collected in three fractions by progressive evaporation of the solvent under reduced pressure: F1, 0·7 g.; F2, 0·8 g.; F3, 0·35 g. All had m. p. 208—209° with shrinkage at 205°. The salt was very insoluble, and specific rotations, measured in dioxan, showed no significant difference, $[\alpha]_D$ +29·0° to +29·5° (*c*, 0·25, room temp.). Three crystallisations of F1 from absolute ethanol gave a salt (0·25 g.), m. p. 208—209°, $[\alpha]_D$ +29·1°, and four recrystallisations of the combined F2 and F3 gave identical material, $[\alpha]_D$ +29·0°. In all, ten different fractions of *salt* were examined, and $[\alpha]_D$ fell between +29·0° and +30·1° (Found: C, 62·6; H, 4·76. $C_{19}H_{13}O_2Sb,C_8H_{11}N$ requires C, 62·8; H, 4·69%).

Ephedrine salt. The acid (2·0 g.) was dissolved by warming it in a solution of ephedrine (0·9 g.) in ethanol (20 c.c.). After 2 hours a first fraction of salt (0·2 g.), m. p. 184—185°, $[\alpha]_D$ +5·67°, had separated, and after a further 10 hours a second fraction (1·5 g.), m. p. 184—185°, $[\alpha]_D$ +5·40°, was collected. Reduction of the volume of ethanol to 5 c.c. then yielded (after 8 hours) a third fraction (0·8 g.), m. p. 183—184°, $[\alpha]_D$ +5·0°. Four recrystallisations of the combined first and second fractions from absolute ethanol gave 0·5 g., m. p. 184—185°, $[\alpha]_D$ +5·47°. Acid regained from this, and also from the salt obtained after three recrystallisations of the third fraction from the original preparation, was inactive in solution in pyridine. The rotations of the *salts* (Found: C, 60·27; H, 5·4. $C_{19}H_{13}O_2Sb,C_{10}H_{15}ON,H_2O$ requires C, 60·25; H, 5·2%) were measured in dioxan at room temperature (*c*, 0·25) and the ephedrine used had $[\alpha]_D$ −14·85° (*c*, 0·505 in dioxan).

Quinine salt. The acid (2·0 g.) and anhydrous quinine (1·6 g.) were dissolved together in a warm mixture of ethanol (20 c.c.) and chloroform (20 c.c.). After 2 hours the salt, in the form of rosettes of small needles (1·1 g.), was filtered off, and the filtrate when kept overnight deposited a second fraction (2·2 g.). The first fraction, m. p. 203—205° (shrinking at 201°), had $[\alpha]_D$ −94·4° (*c*, 0·5 in " AnalaR " chloroform) and was unaltered by two recrystallisations from ethanol containing a little chloroform. The second fraction from the original preparation had m. p. 199—200°, $[\alpha]_D$ −93·6°, and three recrystallisations effected purification but no

separation of stereoisomers, as the final salt had m. p. 203—205°, $[\alpha]_D$ −94·7°. In all, ten different fractions of *salt* (Found: C, 65·0; H, 5·2. $C_{19}H_{13}O_3Sb$,$C_{20}H_{24}O_3N_2$ requires C, 65·1; H, 5·2%) were examined; they showed no significant difference in $[\alpha]_D$, and acid regained from three of these fractions was inactive in pyridine.

9-p-*Carbethoxyphenyl*-2-*nitro*-9-*stibiafluorene* (III; R = CO_2Et, R′ = NO_2).—The reaction of the antimony chloride double salt of diazotised 2-amino-4′-nitrodiphenyl (10·7 g., 0·05 mol.) in ethanol with *p*-carbethoxyphenylstibonous chloride gave *p*-carbethoxyphenyl-2-4′-nitrodiphenylylstibine trichloride (18 g.), m. p. 88—94° after crystallisation from ethanol containing a little hydrochloric acid. The compound contains solvent of crystallisation and was not analysed, but on reduction with stannous chloride gave p-*carbethoxyphenyl*-2-4′-*nitrodiphenylylstibinous chloride*, m. p. 156—157° (Found: C, 49·5; H, 3·9; Sb, 24·25. $C_{21}H_{17}O_4NClSb$ requires C, 49·9; H, 3·4; Sb, 24·1%). The stibinic acid (8 g.) obtained from the crude trichloride was subjected to the usual cyclisation procedure but even after prolonged heating on a water-bath only a small yield (0·8 g.) of 9-p-*carbethoxyphenyl*-2-*nitro*-9-*stibiafluorene*, m. p. 193·5—195° was obtained (Found: C, 53·7; H, 3·5; Sb, 26·2. $C_{21}H_{16}O_4NSb$ requires C, 53·9; H, 3·45; Sb, 26·0%). The bulk of the material was regained as the stibinous chloride, m. p. 156—157°. Hydrolysis of the cyclic ester gave 9-p-*carboxyphenyl*-2-*nitro*-9-*stibiafluorene* (III; R = CO_2H, R′ = NO_2) as a yellow powder, m. p. 212·5—213·5° (blackening) (Found: C, 52·3; H, 3·1. $C_{19}H_{12}O_4NSb$ requires C, 51·9; H, 2·8%).

2-*Nitro- and* 2-*Amino*-9-p-*tolyl*-9-*stibiafluorene*.—2-Amino-4′-nitrodiphenyl (32·1 g., 0·15 mol.) was converted by the usual series of reactions into 2-4′-*nitrodiphenylyl*-p-*tolylstibine trichloride* (I; R = Me, R′ = NO_2), m. p. 160—162° (22·2 g., 29%) (Found: C, 43·9; H, 2·9. $C_{19}H_{15}O_2NCl_3Sb$ requires C, 44·1; H, 2·9%). The corresponding stibinic acid was cyclised to the stibiafluorene very slowly, and good yields were obtained only when the reaction was allowed to proceed for a period considerably longer than the 3 hours found sufficient in previous cyclisations. When the stibinic acid (21 g.) was dissolved in freshly distilled acetic anhydride (450 c.c.) containing sulphuric acid (1 c.c.) and heated on a boiling-water bath for 4 hours, then poured into water (2 l.), the filtered precipitate was only partly soluble in acetone (50 c.c.). The insoluble portion was shown to be unchanged stibinic acid and not the stibiafluorene oxide, the solubilities being the reverse of those found in the cyclisation of the stibinic acid from (I; R = CO_2Et, R′ = H). Reduction of the insoluble portion (7·1 g.) in a mixture of acetone and 3N-hydrochloric acid with stannous chloride (7 g.) readily gave 2-4′-nitrodiphenylyl-*p*-tolylstibinous chloride, m. p. 147—148°. Addition of stannous chloride to the acetone solution of the soluble fraction gave immediately a pale yellow crystalline deposit of 2-*nitro*-9-p-*tolyl*-9-*stibiafluorene*, m. p. 157—159° (8 g., 50%) after recrystallisation from ethyl acetate, from which it separates as yellow needles (Found: C, 55·75; H, 3·49; Sb, 29·8. $C_{19}H_{14}O_2NSb$ requires C, 55·65; H, 3·44; Sb, 29·7%). When the period of heating was increased to 8 hours the yield was increased to 62%.

Reduction of the nitro- to the amino-group with stannous chloride in ethanol and hydrochloric acid was unsatisfactory, and an attempt to reduce with zinc and alkali gave a very insoluble orange substance, presumably an azo-compound. Satisfactory reduction occurred under the neutral conditions recommended for the preparation of 2-aminofluorene (*Org. Synth.*, Vol. II, p. 448). A solution of the nitro-compound (3·5 g.) in aqueous ethanol (120 c.c.; EtOH : H_2O = 5 : 1) was heated on a boiling-water bath for 4 hours with zinc dust (20 g.) and calcium chloride (2 g.). The filtered solution was evaporated to 40 c.c. and, on cooling, 2-*amino*-9-p-*tolyl*-9-*stibiafluorene* (III; R = Me, R′ = NH_2) (2·9 g.) crystallised as rosettes of pale cream needles, m. p. 132—133° (Found: C, 59·9; H, 4·8; Sb, 32·25. $C_{19}H_{16}NSb$ requires C, 60·0; H, 4·24; Sb, 32·0%).

Resolution of (±)-2-*Amino*-9-p-*tolyl*-9-*stibiafluorene*.—Small-scale tests indicated that the (±)-base formed salts with (+)-camphorsulphonic, (+)-tartaric, dibenzoyltartaric, and (−)-malic acids. The salts obtained from the last two acids were inhomogeneous, containing crystals of the free amine. The (+)-camphorsulphonate on crystallisation gave fractions ranging from $[\alpha]_D$ +18·6° to $[\alpha]_D$ +14·7° (*c*, 1·0 in absolute ethanol), all of which mutarotated to a constant value of $[\alpha]_D$ +12·5° overnight, and optically inactive base was obtained from the two extreme fractions of salt. The hydrogen (+)-tartrate appeared to be the most suitable, and in a first attempt the (±)-amine (3·8 g., 0·01 mol.) in ethanol (50 c.c.) was added to (+)-tartaric acid (1·65 g., 0·011 mol.) in boiling ethanol (20 c.c.), and the solution was filtered from a small gelatinous separation and kept overnight. The properties of the fractions obtained are given in Table 1(*a*); vacuum distillation below 30° was used for evaporation of the mother-liquors, and $[\alpha]_D$ were measured in " AnalaR " acetone between 20° and 23° (*c*, *ca.* 0·5).

The mother-liquors from F3 formed a gel, which was dissolved in ethanol and decomposed with 0·5N-sodium hydroxide, giving a specimen of base, $[\alpha]_D$ −146·5° (*c*, 0·505 in " AnalaR " benzene). Recrystallisation of F1 from ethanol (20 c.c.) gave a fraction of salt A, 0·7 g., $[\alpha]_D$ +206·0°, and similarly F2 gave B, 0·4 g., $[\alpha]_D$ +151·2°. Recrystallisation of A gave 0·4 g. of material, $[\alpha]_D$ +227·5°, but this was obviously a mixture containing pale buff-coloured crystals of the free amine. Recrystallisation of B gave 0·2 g. of salt, m. p. 160—161° (decomp.), $[\alpha]_D$ +216·5°, which later proved to be the optically pure (+)-acid (+)-base salt. The mother-liquors from the crystallisation of B and from the later fractions of A formed gels.

TABLE 1.

(*a*)	Vol. of solution (c.c.)	Time of standing (hrs.)	Wt. (g.)	$[\alpha]_D$	M. p.
F1	70	18	1·85	+26·6°	154° (decomp.)
F2	20	2·5	1·50	−12·0	145—148 (decomp.)
F3	15	0·5	0·32	−83·3	125—142 ,,
(*b*)					
X1	110	22	7·0	+43·4	156° (decomp.)
X2	30	7	2·4	−20·85	128—144
X3	0	—	0·9	−95·0	101—132

In a second resolution the (±)-base (7·6 g.) in ethanol (90 c.c.) was added to a solution of 3·3 g. of (+)-tartaric acid in 20 c.c. of boiling ethanol, and the fractions obtained are listed in Table 1(*b*). Two recrystallisations of X1 gave a fraction of salt Y (2·25 g.), $[\alpha]_D$ +192·0°, and two further recrystallisations of Y from ethanol (20 c.c.) containing (+)-tartaric acid (0·5 g.) gave the (+)-acid (+)-base *salt* as opaque needles, 1·2 g., m. p. 161—162° (decomp.), $[\alpha]_D$ +217·0°, unchanged by further crystallisation (Found: C, 52·4; H, 4·0. $C_{19}H_{16}NSb,C_4H_6O_6$ requires C, 52·1; H, 4·2%). On progressive evaporation of the mother-liquor from Y, a fraction of salt, $[\alpha]_D$ +52·5°, was obtained, followed by a separation of the free *amine*, $[\alpha]_D$ −66·9°, m. p. 131—134° (Found: C, 60·2; H, 4·6. $C_{19}H_{16}NSb$ requires C, 60·0; H, 4·2%).

Recovered base (2 g., $[\alpha]_D$ −30°, approx.) in ethanol (20 c.c.) was added to a hot solution of (−)-tartaric acid (1 g.) in ethanol (10 c.c.) and set aside for 18 hours. The first fraction of salt, 1·12 g., m. p. 145—149°, $[\alpha]_D$ −94·2°, was twice recrystallised from ethanol containing a little (−)-tartaric acid and gave (−)-acid (−)-base *salt*, 0·25 g., m. p. 160—161° (decomp.), $[\alpha]_D$ −212·8°, unchanged in $[\alpha]_D$ on recrystallisation (Found: C, 52·7; H, 4·4%). The rotation of this salt is lower than that of its enantiomer because the (−)-tartaric acid was not quite optically pure, but also the recovered base from which the salt was prepared was brown and a faint colour persisted in the salt in contrast to the colourless enantiomer.

Isolation of (+)- *and* (−)-2-*Amino*-9-p-*tolyl*-9-*stibiafluorene*.—Treatment of a solution of the (+)-acid (+)-base salt (0·5 g.) in ethanol (25 c.c.) with 0·5N-sodium hydroxide at −10° gave a crystalline precipitate of (+)-2-*amino*-9-p-*tolyl*-9-*stibiafluorene* as fine cream needles (0·32 g.), m. p. 136—138°, $[\alpha]_D^{22}$ +250·5°±1° (*c*, 0·530 in " AnalaR " benzene), +213·5°±2° (*c*, 0·281 in " AnalaR " chloroform) (Found: C, 60·35; H, 4·5. $C_{19}H_{16}NSb$ requires C, 60·0; H, 4·2%). Decomposition of the salt without cooling, or in acetone solution, gave specimens of the base which were less optically pure and had $[\alpha]_D$ ranging from +230° to 245°. Decomposition of the (−)-acid (−)-base salt by the same method gave (−)-base, m. p. 136—138°, $[\alpha]_D^{23}$ −248·0°±2° (*c*, 0·248 in " AnalaR " benzene). The m. p.s of the enantiomeric amines when observed in a capillary tube ranged from 125° to 140° when the bath was warmed from room temperature, and from 135° to 142° when the capillary was inserted at 130°. The m. p. quoted above, *viz.*, 136—138°, was observed by microscope when crystals were dropped on to a Kofler hot-stage at 130° and the temperature was raised 3° per minute.

Racemisation of the (+)-*Amine*.—The (+)-amine (*ca.* 0·1 g.) was dissolved in " AnalaR " benzene at the required temperature and made up to 20 c.c., and the racemisation was observed in a water-jacketed polarimeter tube (l = 2). The rate constants were evaluated graphically and the results are summarised in Table 2. In Expt. 3, 0·0991 g. of (+)-amine was used, and the initial α_D 2·46° fell to 2·10° in 8 hours. The water-circulating pump ceased overnight and the temperature in the polarimeter tube fell to 22°. The value α_D 1·495° was observed when the solution had regained 30·1° and was used as the initial rotation. The solution, α_D +0·36°, was optically inactive when observed 10 weeks later. The specimens of (+)-amine used in Expts. 3 and 4 were obtained from the same (+)-acid (+)-base salt by decomposition in the same way but at different times. The only observed difference in treatment was in the time of drying *in vacuo*. The solution from Expt. 5 was boiled under reflux for 8 hours and was then optically inactive. The base recovered from the solution as a yellow scale had m. p. 127—

TABLE 2.

Expt.	Temp.	Wt. (g.)	Initial α_D	Final α_D	Time (hr.)	100k *	Half-life (hr.)
(+)-Amine.							
1	22·0°	0·1028	2·58°	0·65°	119·5	1·15	60·3
2	25·4°	0·1019	2·55	0·50	102	1·61	42·9
3	30·1°	—	1·495	0·36	68	2·02	34·3
4	30·8°	0·0511	1·28	0·52	28·75	3·15	22·0
5	40·0°	0·0912	2·20	0·23	45	5·16	13·4
(−)-Amine.							
	23°	0·0496	−1·23	−0·46	100	0·98	70·5
(+)-Amine in pyridine.							
	23°	0·0507	1·26	0·255	58	2·73	25·4

* $k = (1/t) \ln \alpha_0/\alpha_t$ (in hr.$^{-1}$).

131° (Found: C, 60·45; H, 4·6%), and recrystallisation from aqueous ethanol raised the m.p. to 131—132°.

(+)-Amine (0·0562 g.) was dissolved in " AnalaR " chloroform and the solution, α_D +1·20°, was shaken with 4N-hydrochloric acid (2 × 20 c.c.). The chloroform solution was rapidly dried (Na_2SO_4), examined 20—25 minutes after acid treatment, and found to have α_D +0·03°. Removal of the chloroform on a water-bath left a brown glass, which with alkali gave a powder, m. p. 70—91°, and m. p. 120—127° after recrystallisation, indicating considerable decomposition.

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853. *The Cyanoethylation of Aryl Phosphines.*

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Cyanoethylation of phenylphosphine and of diphenylphosphine occurs readily without use of a catalyst, whereas that of aniline and diphenylamine is vigorously promoted by an acidic catalyst, and that of phenylarsine by a basic catalyst.

The chemical properties of bis-2-cyanoethylphenylphosphine $Ph{\cdot}P(CH_2{\cdot}CH_2{\cdot}CN)_2$ and of 2-cyanoethyldiphenylphosphine $Ph_2P{\cdot}CH_2{\cdot}CH_2{\cdot}CN$ have been investigated. These compounds, and also 2-carboxyethyldiphenylphosphine, could not be cyclised to keto-phosphines: in this respect they are similar to their arsenic analogues, but differ markedly from their nitrogen analogues.

IT has been shown by R. C. Cookson and Mann (*J.*, 1947, 618; 1949, 67) that combination of aniline and vinyl cyanide, to give *NN*-bis-2-cyanoethylaniline, $Ph{\cdot}N(CH_2{\cdot}CH_2{\cdot}CN)_2$, occurs readily only when the reactants are heated in the presence of acetic acid at 150°, and that the similar conversion of diphenylamine into *N*-2-cyanoethyldiphenylamine, $Ph_2N{\cdot}CH_2{\cdot}CH_2{\cdot}CN$, requires heating in the presence of acetic acid, copper acetate, and metallic copper at 150° (cf. also Braunholtz and Mann, *J.*, 1952, 3046). On the other hand, although the corresponding conversion of phenylarsine and diphenylarsine into bis-2-cyanoethylphenylarsine and 2-cyanoethyldiphenylarsine respectively occurs readily when the reactants are boiled under reflux in the absence of a catalyst, the reaction of the phenylarsine in particular becomes very vigorous in the presence of an alkaline catalyst.

We have therefore investigated the cyanoethylation of the intermediate phenylphosphine and diphenylphosphine. When a mixture of phenylphosphine and an excess of vinyl cyanide was heated at 130—135° for 6 hours, bis-2-cyanoethylphenylphosphine, $Ph{\cdot}P(CH_2{\cdot}CH_2{\cdot}CN)_2$, was formed in 62% yield, calculated on the purified product. Addition of acetic acid to the reaction mixture caused no significant change in yield, but

the crude product was now apparently purer, since it could be purified by crystallisation without intermediate distillation. Addition of a trace of sodium methoxide to the reaction mixture, however, decreased the yield to 49%.

Similarly a mixture of diphenylphosphine and vinyl cyanide when heated at 130° for 7 hours gave 2-cyanoethyldiphenylphosphine in 71% yield, which was not appreciably affected by the addition of acetic acid, but the presence of sodium methoxide in the reaction mixture caused the yield to fall to 43%.

These results indicate that the cyanoethylation of primary and secondary phosphines does not require a catalyst, and that the process is thus truly intermediate between the acid-catalysed cyanoethylation of amines and the base-catalysed cyanoethylation of arsines. It also appears probable that the mechanism of the process cannot be the same with the three classes of compound.

We have investigated the properties of the new 2-cyanoethylphosphines. Bis-2-cyanoethylphenylphosphine forms colourless crystals, and has been characterised as the crystalline methiodide and the palladobromide complex $[\{Ph\cdot P(CH_2\cdot CH_2\cdot CN)_2\}_2PdBr_2]$. The phosphine does not form a stable picrate : this is not unexpected, for Braunholtz and Mann (*loc. cit.*) were unable to isolate the picrate of *NN*-bis-2-cyanoethylaniline.

Acid or alkaline hydrolysis of the phosphine furnished bis-2-carboxyethylphenylphosphine, $Ph\cdot P(CH_2\cdot CH_2\cdot CO_2H)_2$, but neither this acid nor its derivatives with potassium palladobromide or palladochloride, or with methyl iodide, could be obtained crystalline. It is noteworthy that Cookson and Mann (*loc. cit.*, 1949) also obtained the corresponding nitrogen derivative as a viscous syrup.

The crystalline 2-cyanoethyldiphenylphosphine has also been characterised as its methiodide and its palladobromide complex : on hydrolysis it readily furnishes the crystalline 2-carboxyethyldiphenylphosphine, $Ph_2P\cdot CH_2\cdot CH_2\cdot CO_2H$, which gives a simple yellow palladobromide complex, $[(C_{15}H_{15}O_2P)_2PdBr_2]$, and an orange-red binuclear complex, $[(C_{15}H_{15}O_2P)_2(PdBr_2)_2]$.

The above cyano- and carboxy-phosphines complete three new eutropic series, the melting points of which are given in the Table.

X	$Ph\cdot X(CH_2\cdot CH_2\cdot CN)_2$	$Ph_2X(CH_2\cdot CH_2\cdot CN)$	$Ph_2X(CH_2\cdot CH_2\cdot CO_2H)$
N	81°	41°	112°
P	73	64	126
As	60	38	105

It is noteworthy that *NN*-bis-2-cyanoethylaniline undergoes cyclisation under the influence of aluminium chloride to form 1 : 6-diketojulolidine (Mann and Smith, *J.*, 1951, 1898), and 2-carboxyethyldiphenylamine similarly, when treated with phosphoric anhydride in boiling xylene, gives 1 : 2 : 3 : 4-tetrahydro-4-keto-1-phenylquinoline (Cookson and Mann, *loc. cit.*; Mann, *J.*, 1949, 2816). On the other hand, attempts to carry out similar cyclisations of bis-2-cyanoethylphenylarsine, 2-cyanoethyldiphenylarsine, and 2-carboxyethyldiphenylarsine failed, in spite of a variety of conditions employed (Cookson and Mann, *loc. cit.*). We have now attempted the cyclisation of the phosphorus analogues of these three arsine compounds, but again without success. Of the compounds shown in the above Table, therefore, cyclisation to the corresponding ketones appears to be limited to the nitrogen derivatives.

Since some tertiary phosphines are more strongly basic than the corresponding amines (Davies and Addis, *J.*, 1937, 1622), it is possible that phenylphosphine is also more basic than aniline, although apparently no quantitative data are available. Phenylphosphine, however, when heated with acetic anhydride gives the diacetyl derivative, which we have been unable to obtain crystalline although it is a stable compound in the absence of water, and can be distilled without decomposition. This compound therefore has also been characterised as its crystalline palladobromide complex, of composition $[(Ph\cdot PAc_2)_2PdBr_2]$.

Experimental

Phenylphosphine was prepared as described by Mann and Millar (*J.*, 1952, 3039) and stored in sealed weighed ampoules.

Bis-2-cyanoethylphenylphosphine.—(a) *No catalyst.* Phenylphosphine (4·1 g.) and vinyl

cyanide (5·9 g., 3 mols.) were added to turn to a glass tube previously cooled in solid carbon dioxide and filled with nitrogen, the tube being then sealed. This technique was employed in order to reduce to a minimum both the foul odour and possible oxidation of the phosphine. The tube was then heated at 130—135° for 6 hours, the mixture forming a pale yellow oil. The cold product, when seeded with the pure tertiary phosphine crystallised, but repeated recrystallisation of this material did not give a pure product. The crude product was therefore distilled, the principal fraction of the phosphine having b. p. 195—205°/0·2 mm., leaving a dark non-volatile residue. The distilled *phosphine* readily crystallised, and when recrystallised from ethanol formed colourless crystals (5 g., 62%), m. p. 72—73° (Found: C, 66·4; H, 5·8; N, 1·29. $C_{12}H_{13}N_2P$ requires C, 66·6; H, 6·05; N, 12·95%).

(b) *Acid catalyst.* Phenylphosphine (2 g.), vinyl cyanide (2·9 g., 3 mols.), and acetic acid (4 c.c.) were treated as above. Excess of solvent was removed by distillation from the syrupy product, and the residue then shaken with saturated aqueous sodium carbonate. The semi-solid product was purified directly by recrystallisation from ethanol: one recrystallisation gave the phosphine, m. p. 68—71° (2·36 g., 60%).

(c) *Basic catalyst.* A mixture of the phosphine (5·5 g.), vinyl cyanide (8 g., 3 mols.), and sodium methoxide (*ca.* 0·005 g.) was heated as in (a). Distillation gave the phosphine (5·25 g., 49%), m. p. 72—73° after recrystallisation from ethanol.

A solution of the phosphine in methyl iodide, when warmed and cooled, deposited the *methiodide*, colourless crystals (from ethanol), m. p. 115° (Found: C, 43·7; H, 4·2; N, 7·75. $C_{13}H_{16}N_2IP$ requires C, 43·6; H, 4·5; N, 7·8%). The methopicrate was not precipitated when ethanolic solutions of this salt and of sodium picrate were mixed.

When an ethanolic solution of a small excess of the phosphine and an aqueous ethanolic potassium palladobromide solution were mixed, boiled, and cooled, lemon-yellow crystals of *dibromodi(bis-2-cyanoethylphenylphosphine)palladium* were deposited, having m. p. 227—228° after recrystallisation from aqueous acetone (Found: C, 41·3; H, 3·4; N, 7·9. $C_{24}H_{26}N_4Br_2P_2Pd$ requires C, 41·2; H, 3·75; N, 8·0%).

Oxidation. An acetone solution of the phosphine was treated at 60° with an excess of hydrogen peroxide, set aside overnight, and then evaporated in a vacuum. The residual crystalline oxide was very soluble in polar solvents and could not be satisfactorily recrystallised.

Hydrolysis. (*a*) The solution of the phosphine in aqueous-ethanolic potassium hydroxide was boiled under reflux in a nitrogen atmosphere. The cold solution was acidified with hydrochloric acid, and the solvent removed under reduced pressure in nitrogen. The residue was extracted with acetone, which on evaporation gave a syrup which could not be induced to crystallise.

(*b*) The phosphine was similarly hydrolysed with concentrated hydrochloric acid; evaporation in a vacuum followed by extraction of the residue with boiling ethanol again afforded a syrup which could not be crystallised.

Diphenylchlorophosphine.—The following modification of Michaelis's method (*Ber.*, 1877, **10**, 627; Michaelis and Link, *Annalen*, 1881, **207**, 208) was found to give the highest yield. A mixture of phenyldichlorophosphine (130 g.) and pure dry diphenylmercury (165 g., 0·64 mol.) was heated in an oil-bath under a slow stream of nitrogen at 200° for 90 minutes with occasional vigorous shaking. Light petroleum (500 c.c.; b. p. 60—80°) was added to the warm reaction mixture, which was boiled for 10 minutes, and the petroleum then decanted. The viscous residue was mixed with half its bulk of dry sand, and the petroleum extraction repeated. Finally the residue was thoroughly kneaded with warm petroleum, transferred to a Buchner funnel, and there sucked as free from petroleum as possible whilst being pressed firmly on to the filter. The solvent from the combined extracts was distilled under nitrogen, and the residue, when fractionated under reduced pressure, gave (*a*) an early fraction of phenyldichlorophosphine (*ca.* 40 c.c.), (*b*) diphenylchlorophosphine, b. p. 178—180°/18 mm. (55 g., 54%). This colourless liquid contained a trace of suspended mercury, which settled out when set aside overnight. Omission of the treatment with sand gave reduced yields (*ca.* 10%), because the reaction product is not readily wetted by petroleum.

Diphenylphosphine.—Malatesta (*Gazzetta*, 1947, **77**, 518) has described the preparation of this phosphine in 40% yield by the action of a considerable excess of phenylmagnesium bromide on tetraphosphorus trisulphide. We have, however, obtained by this method only a low yield of the phosphine contaminated by sulphur derivatives. The following modification of Dörken's method (*Ber.*, 1888, **21**, 1505; cf. also Michaelis and Gleichmann, *Ber.*, 1882, **15**, 801) appears to be the most satisfactory, the reaction involved being formulated by Dörken as:

$$4Ph_2PCl + 3Na_2CO_3 + H_2O = 2Ph_2PH + 2Ph_2PO_2Na + 3CO_2 + 4NaCl$$

Diphenylchlorophosphine (50 g.) was added dropwise during 30 minutes to an agitated solution of anhydrous sodium carbonate (25 g.) in water (80 c.c.) contained in a flask which was fitted with a stirrer, dropping funnel, and reflux condenser, and into which nitrogen was passed throughout the preparation. Carbon dioxide was smoothly evolved and oily drops of the phosphine separated in the solution. The latter was finally warmed to 50° and the mixture stirred for a further 30 minutes. The phosphine was then extracted with benzene, and the extract dried ($CaCl_2$) and fractionally distilled at atmospheric pressure in a stream of nitrogen. The phosphine was obtained as a colourless liquid, b. p. 280—282° (10 g., 47%), and sealed under nitrogen in weighed ampoules.

2-Cyanoethyldiphenylphosphine.—(a) *No catalyst.* A mixture of diphenylphosphine (3·3 g.) and vinyl cyanide (1·9 g., 2 mols.) in a sealed tube, as previously described, was heated at 130° for 7 hours. Distillation of the excess of vinyl cyanide under nitrogen gave a residue which solidified on cooling and when twice recrystallised from methanol gave the *phosphine* as colourless crystals (3 g., 71%), m. p. 64—64·5° (Found: C, 75·5; H, 5·9; N, 5·7. $C_{15}H_{14}NP$ requires C, 75·3; H, 5·9; N, 5·85%). The combined mother-liquors from the recrystallisations were evaporated and the residue was hydrolysed, as described below, to the corresponding acid (0·9 g.), m. p. 124—125°.

(b) *Acid catalyst.* Repetition of the above experiment with the addition of acetic acid (4 c.c.) to the reaction mixture gave the phosphine (2·86 g., 68%), m. p. 63—64°.

(c) *Basic catalyst.* A mixture of diphenylphosphine (6·2 g.), vinyl cyanide (3·5 g., 2 mols.), and sodium methoxide (0·005 g.), when treated as before, gave the required phosphine, which, similarly recrystallised from methanol, also had m. p. 64—64·5° (mixed and unmixed) (3·4 g., 42·5%).

When methyl iodide was added to an ethereal solution of the phosphine, the *methiodide* was slowly deposited as colourless crystals, m. p. 163—164° (Found: C, 50·7; H, 4·5; N, 3·9. $C_{16}H_{17}NIP$ requires C, 50·4; H, 4·5; N, 3·7%). The methopicrate of this salt also could not be prepared in ethanolic solution.

Dibromobis-2-cyanoethyldiphenylphosphine-palladium, prepared as the previous palladium derivative, formed yellowish-brown crystals, m. p. 176°, from ethanol (Found: C, 48·0; H, 4·0; N, 4·1. $C_{30}H_{28}N_2Br_2P_2Pd$ requires C, 48·4; H, 3·8; N, 3·8%).

Hydrolysis. The phosphine (0·48 g.) was added to a solution of potassium hydroxide (0·44 g., 4 mols.) in 50% aqueous ethanol (4·4 c.c.), which was boiled under reflux in a nitrogen atmosphere for 3 hours. The ethanol was then distilled off, and the residual solution diluted with water, cooled, and made just acid to litmus. The precipitated crystalline *2-carboxyethyldiphenylphosphine*, when recrystallised from aqueous ethanol, formed colourless crystals, m. p. 125—127° (Found: C, 69·6; H, 5·6. $C_{15}H_{15}O_2P$ requires C, 69·75; H, 5·9%).

A solution of the acid in aqueous ethanol did not affect Congo-red or evolve carbon dioxide from sodium hydrogen carbonate solution. The acid when dissolved in hot methyl iodide gave an oil which could not be recrystallised.

Dibromobis-2-carboxyethyldiphenylphosphine-palladium was formed when theoretical quantities of the acid and of potassium palladobromide were heated together in boiling ethanol; it formed yellow crystals (from ethanol), m. p. 226—228° (decomp.) (Found: C, 46·2; H, 4·2. $C_{30}H_{30}O_4Br_2P_2Pd$ requires C, 46·0; H, 3·9%).

Dibromobis-2-cyanoethyldiphenylphosphine-μ-dibromopalladium was formed when the acid was similarly treated with an excess of potassium palladobromide, and when recrystallised from methanol formed orange-red crystals, m. p. 239—241° (decomp.) (Found: C, 34·1; H, 3·1. $C_{30}H_{30}O_4Br_4P_2Pd_2$ requires C, 34·3; H, 2·9%).

Attempted Cyclisations.—Since all the attempted cyclisations failed, only a general account of the methods employed is given.

(1) *Bis-2-cyanoethylphenylphosphine.* A solution of this compound in chlorobenzene containing an excess of aluminium chloride was boiled under reflux for 8 hours, but the unchanged phosphine (54%) was subsequently recovered.

(2) *2-Cyanoethyldiphenylphosphine.* (*a*) An experiment similar to (1) ultimately gave the unchanged phosphine (73%). (*b*) The phosphine was added to a fused mixture of aluminium chloride, potassium chloride, and sodium chloride, which was then heated at 175° for 3 hours (cf. F.P. 806,715), but no ketonic product could be isolated.

(3) *2-Carboxyethyldiphenylphosphine.* (*a*) A solution of the acid in xylene, containing phosphoric anhydride and "Hyflo Supercel" in suspension was boiled for 3 hours under reflux in nitrogen. The unchanged acid (14%) was subsequently recovered, in addition to oily products which could not be purified. (*b*) A solution of the acid in benzene was heated first with

phosphorus pentachloride and then with aluminium chloride. Working up gave a small yield of crude 2-benzoylethyldiphenylphosphine oxide, identified as its 2 : 4-*dinitrophenylhydrazone*, yellow-orange crystals (from ethanol), m. p. 234—236° (decomp.) (Found : C, 63·05; H, 4·65; N, 11·4. $C_{27}H_{23}O_5N_4P$ requires C, 63·0; H, 4·5; N, 10·9%). There are many examples of acyl chlorides giving cyclic ketones in benzene solution : in this case, the preferential reaction of the chloride with the solvent confirms the difficulty of the desired cyclisation.

PP-*Diacetylphenylphosphine*.—A mixture of phenylphosphine (2 g.) and acetic anhydride (4 c.c.) in a sealed tube under nitrogen was heated at 130° for 6 hours, giving a colourless liquid free from the odour of unchanged phosphine. The excess of anhydride was removed under reduced pressure, giving a pale amber residual syrup which had a characteristic odour, and could not be crystallised. It distilled without decomposition (b. p. *ca.* 200°/14 mm.), leaving a non-volatile residue, but the distillate did not crystallise. The identity of this (presumably impure) diacetylphenylphosphine was determined by (*a*) its apparent failure to combine with methyl iodide, and (*b*) formation, in hot ethanolic solution, of *dibromobisdiacetylphenylphosphinepalladium*, chocolate brown crystals (from aqueous ethanol), m. p. 183—185° (preliminary decomp.) (Found : C, 37·5; H, 3·65. $C_{20}H_{22}O_4Br_2P_2Pd$ requires C, 37·0; H, 3·4%).

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854. *Acylation and Allied Reactions catalysed by Strong Acids. Part VII.* Evidence for the Existence of Sulphonyl Cations* ($R{\cdot}SO_2^+$).

By H. BURTON and H. B. HOPKINS.

Previous results (*J.*, 1945, 14) on the reaction between sulphonyl chlorides and the dimethoxybenzenes in the presence of zinc chloride are explained by postulating the intermediate production of sulphonyl cations ($R{\cdot}SO_2^+$). "Sulphonyl perchlorates" ($R{\cdot}SO_2^+ClO_4^-$) are shown to be formed less readily, and to be less active, than the "acyl perchlorates." Sulphones are obtained under suitable experimental conditions, showing the existence of the sulphonyl cations : the yields are, however, generally not good.

It was shown by Burton and Hoggarth (*J.*, 1945, 14) that sulphonyl chlorides ($R{\cdot}SO_2Cl$) react with the dimethoxybenzenes in presence of zinc chloride in one or both of two ways, namely, elimination of hydrogen chloride to give the dimethoxyphenyl sulphone, $R{\cdot}SO_2{\cdot}C_6H_3(OMe)_2$, or elimination of methyl chloride to yield the methoxyphenyl sulphonate, $R{\cdot}SO_2{\cdot}O{\cdot}C_6H_4{\cdot}OMe$. In general the *o*- and *p*-dimethoxybenzenes and the more reactive, especially aliphatic, sulphonyl chlorides gave almost exclusively the esters. In view of the results obtained with mixtures of acetyl chloride or acetic anhydride and zinc chloride (Burton and Praill, *J.*, 1951, 726; 1952, 755) it becomes clear that the above results with sulphonyl chlorides are adequately explained as a consequence of the following series of reactions :

(i) $2R{\cdot}SO_2Cl + ZnCl_2 \longrightarrow (R{\cdot}SO_2^+)_2[ZnCl_4]^{--}$

(ii) $R{\cdot}SO_2^+ + C_6H_4(OMe)_2 \longrightarrow R{\cdot}SO_2{\cdot}C_6H_3(OMe)_2 + H^+$

and/or

(iii) $R{\cdot}SO_2^+ + C_6H_4(OMe)_2 \longrightarrow MeO{\cdot}C_6H_4(\overset{+}{O}Me){\cdot}SO_2R \longrightarrow MeO{\cdot}C_6H_4{\cdot}O{\cdot}SO_2R + Me^+$

(iv) $2H^+ + [ZnCl_4]^{--} \longrightarrow 2HCl + ZnCl_2$

and/or

(v) $2Me^+ + [ZnCl_4]^{--} \longrightarrow 2MeCl + ZnCl_2$.

In accordance with these reactions, *m*-dimethoxybenzene (resorcinol dimethyl ether), which must possess an extremely reactive position at $C_{(4)}$, showed preferential sulphone formation.

* Part VI, *J.*, 1952, 755. The scope of the original investigation has been extended by inserting "and Allied" into the title.

Evidence for the existence of sulphonyl cations has also been adduced by Bourne, Randles, Tatlow, and Tedder (*Nature*, 1951, **168**, 942) who suggest that trifluoroacetic anhydride and sulphonic (or carboxylic) acids give a mixed anhydride, $CF_3{\cdot}CO{\cdot}O{\cdot}X$ ($X = R{\cdot}SO_2$ or $R{\cdot}CO$), which exists to a small degree as the ions X^+ and $CF_3{\cdot}CO_2^-$. We agree with this view but would point out that the implication that sulphonic acids are weak acids is certainly not true. It is possible that sulphonic acids are much weaker acids in, *e.g.*, trifluoroacetic acid than in water, and we assume that this view is implicit in the suggested mechanism. We are informed by one of the authors (Tedder, personal communication) that the production of the mixed anhydride from trifluoroacetic acid and acetic anhydride or from trifluoroacetic anhydride and acetic acid, is a very fast reaction: this would follow from the results obtained by Bourne *et al.*

In view of the successful preparation of "acyl perchlorates" from silver perchlorate and acyl halides (Burton and Praill, *J.*, 1950, 2034; 1951, 529) we decided to investigate the possible extension of the procedure to "sulphonyl perchlorates" ($R{\cdot}SO_2{}^+ClO_4^-$). We realised that in comparison with acyl halides, the sulphonyl halides are much less reactive and this is evident in the experiments we have carried out. Generally, the reaction proceeds slowly and incompletely in a solvent of low dielectric constant, *e.g.*, benzene, and more rapidly but still incompletely in nitrobenzene or nitromethane. Preliminary experiments with benzenesulphonyl chloride and silver perchlorate in mesitylene (or anisole) also showed that dark tarry products, similar to those obtained from the sulphonyl chloride and mesitylene in presence of aluminium chloride, were formed. In order to minimise this type of effect we used *m*-xylene as the reactive hydrocarbon but even then the production of coloured by-products was not prevented. In view of this somewhat unexpected complication we studied initially the amount of silver chloride produced from (*a*) benzene- or *p*-bromobenzene-sulphonyl chloride (1 mol.) and silver perchlorate (1·5 mols.) in benzene at 17—18° during 18 hours and (*b*) benzene- or toluene-*p*-sulphonyl chloride and silver perchlorate in nitrobenzene at 20—21° during 2 hours. The yields of silver chloride were: (*a*) 0·89, 0·6, (*b*) 0·73, 0·85 mol., respectively, indicating that for $Ar{\cdot}SO_2Cl$ the rate of the reaction increases, as expected, in the order of electron release of the group Ar. Thus the rate of reaction (1)

$$Ar{\cdot}SO_2Cl + AgClO_4 \longrightarrow Ar{\cdot}SO_2{\cdot}ClO_4 + AgCl \quad . \; . \; . \; . \; (1)$$

is evidently determined by the ease of separation of the chlorine atom of $Ar{\cdot}SO_2Cl$ as the chloride ion. The results also show quite clearly, again as expected, that the reaction proceeds much more rapidly in the solvent of higher dielectric constant.

We have also determined in several experiments the number of g.-ions of hydrogen in the initial aqueous phase after carrying out a reaction with the sulphonyl perchlorate and an active aromatic compound (Ar'H). We deemed this to be necessary in view of the obvious incompleteness of the reactions studied, since reaction (2) if it occurred exclusively would give rise to 1 g.-ion for each molecule of the perchlorate:

$$Ar{\cdot}SO_2{\cdot}ClO_4 + Ar'H \longrightarrow Ar{\cdot}SO_2Ar' + H^+ + ClO_4^- \quad . \; . \; . \; (2)$$

If the sulphonyl perchlorate were not to react as in (2) then on decomposition with water it would give 2 g.-ions of hydrogen:

$$Ar{\cdot}SO_2{\cdot}ClO_4 + H_2O \longrightarrow Ar{\cdot}SO_3H + HClO_4.$$

The results obtained are only of significance for Ar = Ph and possibly C_6H_4Me, since we were able to show that unchanged sulphonyl chloride was not hydrolysed to any significant extent under the experimental conditions used. (This method was not applicable to methanesulphonyl chloride which underwent partial hydrolysis.) The value obtained averaged *ca.* 1·2 g.-ions per g.-mol. of the sulphonyl perchlorate which may suggest that reaction (1) is faster than reaction (2).

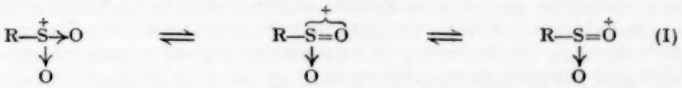
In those cases where a solid product was obtained it proved to be the expected sulphone in accordance with reactions (1) and (2): no other crystalline compound could be isolated. Thus benzenesulphonyl perchlorate and *m*-xylene in benzene, nitrobenzene, or nitromethane gave increasing amounts (7, 15, and 25%, respectively) of pure phenyl *m*-4-xylyl sulphone.

Toluene-*p*-sulphonyl perchlorate and *m*-xylene in nitrobenzene gave 46% of *p*-tolyl *m*-4-xylyl sulphone. In both cases, an identical sulphone was also obtained by the appropriate Friedel–Crafts reaction using aluminium chloride. The last-named sulphone, as obtained in both cases, was found to have m. p. 51—52°, a value which differs widely from that (121°) reported by Meyer (*Annalen*, 1923, **433**, 343), who states that this compound was synthesised by the Friedel–Crafts method and also by passing toluene vapour through *m*-xylene-4-sulphonic acid at 170—180° for 24 hours. We had great difficulty in obtaining crystalline material from the Friedel–Crafts experiment carried out exactly as described by Meyer: we found that a substance other than the true sulphone was produced and although we attach some reserve to our result—in view of the very small amount of the material available—it is probable that some disulphone was also formed. It is also possible that the *m*-xylene used by Meyer was not pure.

In view of the apparent formation of mixtures in our procedure we also investigated the nature of the secondary products. We found that extraction of a chloroform solution of the total reaction product with cold 2N-sodium hydroxide removed small but definite amounts of a phenolic product which may be originally present as such or may have arisen from an easily hydrolysable ester. We were able to prove that some ester was also present in the alkali-washed product since hydrolysis with boiling aqueous-alcoholic potassium hydroxide gave a further quantity of phenolic material and also an acid fraction. It is possible that during the reactions, especially those carried out for 18 hours or so, that the sulphonyl perchlorate is oxidising the aromatic component to a limited extent:

$$R{\cdot}SO_2{}^+ClO_4{}^- + ArH \longrightarrow R{\cdot}SO^+ClO_4{}^- + Ar{\cdot}OH \; (\longrightarrow Ar{\cdot}O{\cdot}SO_2{\cdot}R)$$

It is almost certain that the phenol does not arise from the arylsulphonyl cation since we found that the use of methanesulphonyl perchlorate also led to the formation of phenolic material. Furthermore, the use of nitrobenzene (or benzene) as solvent still resulted in phenol formation. It is also possible that phenol and ester may both arise by the direct attack of the sulphonyl cation on the aromatic component through oxygen, *i.e.*, that the cation exists to a small extent as a hybrid * (cf. I):



(I)

The attack of (I) on ArH would thus lead to Ar·O·SO·R, *i.e.*, an aryl sulphinate, which might be partly hydrolysed by cold, and certainly by hot, 2N-sodium hydroxide. Unfortunately we have not been able to devise a satisfactory method for identifying small amounts of sulphinic and sulphonic acids in admixture.

It will be seen that various by-products are possible and are almost certainly formed: it appears doubtful, therefore, whether the perchlorate technique is really suitable for the preparation of sulphones. The results are however not without some theoretical interest and in view of the fact that one of us is no longer able to take part in the work, we deem it worth while to place them on record.

We have also carried out a few experiments on the reaction of toluene-*p*-sulphinyl chloride on silver perchlorate in *m*-xylene–benzene and find that the reaction is much more rapid than with the sulphonyl chloride. The reaction product was again a viscous gum (? mixture); we were not able to identify *p*-tolyl *m*-4-xylyl sulphoxide as a constituent.

Experimental

Materials.—Silver perchlorate was dried as previously described (*J.*, 1950, 2036). Anisole, mesitylene, *m*-xylene, nitromethane, and nitrobenzene were all dried and redistilled. Benzene was purified by repeated shaking with concentrated sulphuric acid, washed with water, dried, and fractionated (the distillate gave a negative result for thiophen by the isatin test). Benzene-(b. p. 129°/20 mm.) and methane-sulphonyl chloride (b. p. 63·5—64°/19 mm.) were fractionated.

* The work of Bennett and Youle (*J.*, 1938, 1816) and Bennett and Grove (*J.*, 1945, 378) on the formation of phenolic by-products during nitration could be similarly explained by postulating that $NO_2{}^+$ reacts to a small extent in the mesomeric form, $ON{:}O^+$, which would lead to an aryl nitrite and thence the phenol.

Toluene-*p*-sulphonyl chloride was twice recrystallised from light petroleum (b. p. 40—60°) and had m. p. 67·5—68°. *p*-Bromobenzene sulphonyl chloride, similarly purified, had m. p. 74·5—75°. Toluene-*p*-sulphinyl chloride was obtained as a yellow oil from sodium toluene-*p*-sulphinate and thionyl chloride.

General Technique.—Silver perchlorate (7·8 g., 0·0376 g.-mol.) was dissolved in a mixture of the aromatic compound (*e.g.*, *m*-xylene; 20 g., 0·19 g.-mol.) and a diluent (*e.g.*, benzene, 40 g.) and the sulphonyl chloride (0·025 g.-mol.), dissolved in the same diluent (~10 g.), was added gradually to the cooled solution. Silver chloride separated slowly from the reaction mixture which slowly developed a colour (usually reddish). The mixture was then either filtered through a sintered-glass funnel on to crushed ice or poured on to ice and subsequently filtered; in either case, the precipitate of silver chloride was well washed with chloroform and then with water.

The chloroform layer was separated and washed repeatedly (~6 times) with water. These aqueous washings were combined with the main aqueous layer. The chloroform layer was then extracted four times with 2N-sodium hydroxide (except when nitromethane was the diluent), twice more with water, and dried (Na_2SO_4). The chloroform and the other solvents were removed by distillation in a vacuum and the resulting dark oil or gum was kept, or alternatively, refluxed with ~10% aqueous-alcoholic potassium hydroxide. The alcohol was removed by distillation and the residue extracted with chloroform and dried (Na_2SO_4). The dark oil or gum obtained on removal of the chloroform was set aside for several days, or in some cases, weeks, to crystallise. Any solid which separated was filtered off, washed with a little ether, and recrystallised to constant m. p. from aqueous ethanol. The filtrate was evaporated and again left to stand, the process being repeated until no further solid could be obtained.

Treatment of the aqueous layers. All silver ions were removed by addition of excess of sodium chloride solution. Aliquots of the filtrate were titrated to phenolphthalein with 0·1N-sodium hydroxide to determine the number of g.-ions of hydrogen present.

Treatment of the sodium hydroxide extracts. The strongly coloured alkaline extracts were acidified with hydrochloric acid, which discharged most of the colour and gave rise to an immediate turbidity and phenolic odour. In some cases the phenolic compound was isolated as a black gum by ethereal extraction. It amounted to 0·2 g. (expt. 10), 0·1 g. (expt. 12), 0·3 g. (expt. 15).

Treatment of the aqueous layer from the aqueous-alcoholic potassium hydroxide reflux. Acidification with hydrochloric acid caused a turbidity and phenolic odour. Ether-extraction yielded 0·2 g. of a dark oil (expt. 14) and 0·09 g. of a gum (expt. 15) which could be separated by the usual procedure into acid and phenolic fractions.

Further details of some of the experiments are as follows:

Expt. 8. Solid separated from the dark oil (3·4 g.) obtained from benzenesulphonyl chloride and *m*-xylene in nitrobenzene at 22° for 2 hours. Recrystallisation gave colourless plates (0·91 g.) of phenyl *m*-4-xylyl sulphone, m. p. 86° (Found: C, 67·7, 67·5; H, 5·7, 5·9; S, 13·4, 13·4. Calc. for $C_{14}H_{14}O_2S$: C, 68·3; H, 5·7; S, 13·0%). When the experiment was carried out at −1° for 6 hours, 0·7 g. of sulphone, m. p. and mixed m. p. 86°, was obtained. The sulphone obtained from benzenesulphonyl chloride, *m*-xylene, and aluminium chloride in nitrobenzene had m. p. 85—86°, alone or in admixture. Steinkopf and Hübner (*J. pr. Chem.*, **1934**, **141**, 198) give m. p. 87° for the sulphone synthesised from magnesium, bromobenzene, and *m*-xylene-4-sulphonyl fluoride.

Expt. 9. Repetition of expt. 8, with nitromethane as the diluent at 16° for 4·5 hours, gave 1·5 g. of recrystallised sulphone, m. p. and mixed m. p. 85—86°.

Expt. 10. In a modification of expt. 8, benzene was used as the diluent at 18° for 18 hours. The sulphone (0·41 g.) had m. p. and mixed m. p. 86°.

Expt. 18. Toluene-*p*-sulphonyl chloride and *m*-xylene in nitrobenzene at 21° for 2 hours gave an oil (4·3 g.) which gradually deposited crystals (3 g.). Two crystallisations from light petroleum (b. p. 60—80°) gave colourless prisms of *p-tolyl* m-4-*xylyl sulphone*, m. p. 51—52° (Found: C, 69·5; H, 6·3; S, 12·1. $C_{15}H_{16}O_2S$ requires C, 69·2; H, 6·2; S, 12·3%). The same compound was obtained by the Friedel–Crafts procedure from the chloride, *m*-xylene, and aluminium chloride in nitrobenzene.

Control Experiments.—(i) The appropriate amounts of benzenesulphonyl chloride, *m*-xylene, and nitrobenzene dissolved in chloroform were added to an aqueous solution of silver perchlorate. After 1 hour, the mixture was worked up as described above. The chloroform layer gave a mere trace of residue and the aqueous layer contained not more than 0·0004 g.-ion of hydrogen.

(ii) Methane- and benzene-sulphonyl chloride (0·0087 g.-mol.) were dissolved separately in chloroform and poured on to ice. After *ca.* 4 hours the chloroform layer was separated and washed four times with water. The combined aqueous layers were titrated with 0·1N-sodium hydroxide. Hydrolysis of the methanesulphonyl chloride had occurred to the extent of 29% whereas hydrolysis of the benzenesulphonyl chloride was negligible.

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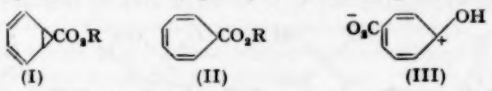
855. *Synthetic Experiments in the* cyclo*Heptatrienone Series. Part II.** 4-*Keto*cyclo*heptatrienecarboxylic Acid.*

By J. R. BARTELS-KEITH, A. W. JOHNSON, and A. LANGEMANN.

The reaction of anisole with ethyl diazoacetate has been investigated as the simplest example of the synthesis of *cyclo*heptatrienone derivatives by the ring expansion of aromatic compounds. Hydrolysis of the ester mixture yields mainly 4-methoxy*cyclo*hepta-1 : 3 : 5-trienecarboxylic acid together with some phenoxyacetic acid, and the action of bromine on the former acid gives 4-keto*cyclo*heptatrienecarboxylic acid, characterised by spectra and its rearrangement with alkali to terephthalic acid. The structure of the 4-methoxy-acid follows from the formation of anisic acid by hydrolysis of the ozonolysis product. By a similar degradation 4-ethoxy*cyclo*hepta-1 : 3 : 5-trienecarboxylic acid, obtained from the methoxy-compound by trans-etherification, yields *p*-ethoxybenzoic acid.

APPLICATION of the diazoacetic ester method of ring expansion of aromatic compounds to the synthesis of tropolones from veratrole and its substitution products has been described in an earlier paper.* The mixed esters produced were only partially purified and the tropolone was then obtained most satisfactorily by oxidation with bromine. The yields of tropolone esters were low, *e.g.*, 7% overall for tropolone-β-carboxylic ester from veratrole, and it seemed probable that, if the tropolone precursor were isolated and identified, the method might be improved.

The pioneer work of Buchner on the condensation of aromatic hydrocarbons with diazoacetic ester (*Ber.*, 1920, **53**, 865, and earlier papers) has established that the product can contain esters (I; R = Et) of the norcaradiene ([4 : 1 : 0]*bicyclo*heptane) type as well as the various *cyclo*heptatriene esters (*e.g.*, II). We investigated the case of anisole first,



(I) (II) (III)

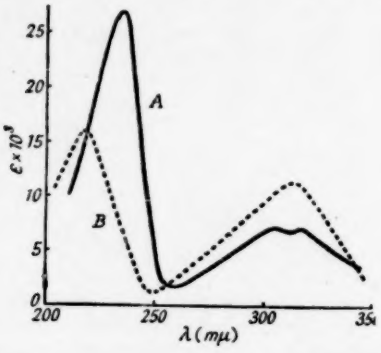
as providing the simplest model of the tropolone synthesis. As expected by analogy with veratrole, anisole reacted with diazoacetic ester, and the product was converted by bromine into a keto*cyclo*heptatrienecarboxylic acid. Since the preliminary announcement of our tropolone synthesis (Bartels-Keith and Johnson, *Chem. and Ind.*, 1950, 677) Doering and Detert (*J. Amer. Chem. Soc.*, 1951, **73**, 876) have briefly described the preparation of *cyclo*heptatrienone itself by a route closely related to the present method, *viz.*, the ring enlargement of anisole with diazomethane followed by treatment of the product with bromine. We have prepared pure intermediary compounds from the crude ester mixture by hydrolysis with ethanolic potassium hydroxide. When the hydrolysis product was acidified directly, either of two acids, A, m. p. 144°, or B, m. p. 188°, depending on the method of acidification, was obtained in some 45% yield, together with tarry by-products. Rapid acidification with concentrated acid gave the latter, and cautious addition of dilute acid the former. Acid A had the formula $C_9H_{10}O_3$, corresponding to the expected methoxy*cyclo*-

* *J.*, 1951, 2352, is taken to be Part I of this series.

heptatrienecarboxylic acid or methoxynorcaradienecarboxylic acid; acid B had the formula $C_{10}H_{12}O_3$, and was also obtained from A by means of ethanol and sulphuric acid. The change therefore involved only the replacement of the methoxyl by an ethoxyl group, as was confirmed by oxidation (see below). If, on the other hand, the hydrolysis product was cooled before acidification, potassium phenoxyacetate crystallised. The significance of this product will be discussed in a later paper.

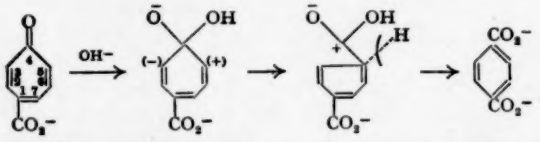
Treatment of acid A or B with bromine gave 4-keto*cyclo*heptatrienecarboxylic acid in high yield. This acid charred but did not melt at 250°, which is in keeping with a tendency to exist in the zwitterion structure (III) as in the case of the pyronecarboxylic acids, and its ultra-violet (see Figure) and infra-red spectra were consistent with the presence of a *cyclo*heptatrienone ring structure.

The position of the carboxyl group in the *cyclo*heptatrienone nucleus was deduced from the formation of terephthalic acid (20%) by the action of aqueous potassium hydroxide; alkaline permanganate also gave terephthalic acid as the sole recognisable product. The mechanism of the alkaline rearrangement bears a formal relation to the benzilic acid change, although an α-diketone is not involved, and the production of terephthalic acid necessitates



Ultra-violet absorption spectra of (*A*) 4-*keto*cyclo*heptatrienecarboxylic acid and* (*B*) 4-*methoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic acid.*

an oxidation at some stage. The initial attack of the hydroxyl ion is probably at $C_{(4)}$ and, in the normal course of the benzilic acid rearrangement, this would be followed by the formation of a bond between $C_{(3)}$ and $C_{(5)}$ with fission of the $C_{(3)}$–$C_{(4)}$ linkage. The final stage necessitates removal of the $C_{(3)}$ hydrogen atom by oxidation. A mechanism involving attack of the hydroxyl ion at $C_{(3)}$ is also possible, ultimately leading to tropolone-γ-carboxylic acid, which might then undergo rearrangement to terephthalic acid. This possi-

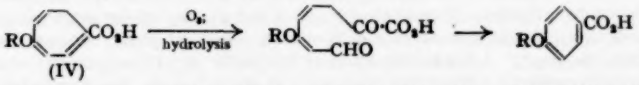


bility is being investigated further. The formation of aromatic carboxylic acids from tropolones by the action of alkali is well established (*e.g.*, Nozoe, *Nature*, 1951, **167**, 1055; Cook and Loudon, *Quart. Reviews*, 1951, **5**, 99) and does not involve oxidation (see also Doering and Knox, *J. Amer. Chem. Soc.*, 1951, **73**, 828). The ease of the rearrangement of 4-keto*cyclo*heptatrienecarboxylic acid which proceeds in alkaline solution at room temperature is in marked contrast to the formation of benzoic acid from tropolone, which requires fusion with potassium hydroxide at 220°. In this case the hydroxyl group has a retarding effect on the change just as carboxyl and nitro-groups favour the formation of aromatic compounds.

The structure of 4-keto*cyclo*heptatrienecarboxylic acid indicates that the methoxy-group (Zeisel) in acid A is also in the 4-position, unless rearrangement occurs during the

bromination, and it will be shown that this is not the case. The structural features of acid A to be determined were therefore the nature of the ring system, whether norcaradiene or *cyclo*heptatriene, and, in the latter case, the position of the double bonds. The ultra-violet absorption spectra of the two acids A and B were very similar but, in the absence of authentic standard compounds, did not permit a choice of ring structure. The infra-red spectra (see Experimental) seemed to offer more promise. Derfer, Pickett, and Boord (*J. Amer. Chem. Soc.*, 1949, **71**, 2482; see also Roberts and Chambers, *ibid.*, 1951, **73**, 5030, 5034; Marrison, *J.*, 1951, 1614) claim that the presence of a *cyclo*propane ring causes a band in the infra-red spectrum between 1000 and 1030 cm.$^{-1}$, and this appears to hold in certain of the more complex derivatives such as the *cyclo*steroids (*e.g.*, Barton, *J.*, 1951, 1444). Unfortunately many groups, including enol ethers, absorb in this region of the spectrum, and a band in this position is not characteristic of the *cyclo*propane ring; thus, although the acids A and B absorb at 1024 and 1034 cm.$^{-1}$ respectively, no decision could be taken on this basis (for the related case of *cyclo*octatetraene see Cope and Burg, *J. Amer. Chem. Soc.*, 1952, **74**, 168).

In the norcaradiene series, structures have been frequently deduced on the basis of the isolation of *cyclo*propane derivatives from oxidations (cf. Braren and Buchner, *Ber.*, 1901, **34**, 982; Buchner and Hediger, *Ber.*, 1903, **36**, 3502; Drake and Sweeney, *J. Org. Chem.*, 1946, **11**, 67). Ozonisation of the acid A and subsequent alkaline oxidative hydrolysis gave anisic acid; this establishes that acid A cannot be a norcaradiene derivative, as no *cyclo*propane derivative was obtained; the acid A must therefore contain the *cyclo*hepta-triene ring system. It also confirms the relative positions of the methoxyl and carboxyl groups. Finally consideration of the mode of formation of anisic acid leaves only one (IV; R = Me) of the seven possibilities for the position of the double bonds in acid A. It is assumed that the initial oxidative attack is at the double bond αβ to the carboxyl group, and that, after hydrolysis, the intermediate formyl-keto-acid undergoes an internal aldol cyclisation to the aromatic acid. This novel formation of an aromatic ring from the products of an ozonolysis can therefore be formulated:



(IV)

The structure of acid B was similarly proved to be (IV; R = Et) by the isolation of *p*-ethoxybenzoic acid after ozonolysis.

Hydrogenation of acid A yielded *cyclo*heptanecarboxylic acid, hydrogenolysis of the methoxyl group having occurred. On the other hand, a similar process gave slightly impure ethoxy*cyclo*heptanecarboxylic acid from acid B.

It therefore follows that in this series at least the immediate precursor of the *cyclo*-hepatrienone derivative is the methoxy*cyclo*heptatrienecarboxylic acid (IV; R = Me), and that good overall yields of the 4-keto*cyclo*heptatrienecarboxylic acid can be obtained if this intermediate product is isolated and purified.

Experimental

M.p.s are uncorrected except where otherwise stated.

Reaction of Anisole and Ethyl Diazoacetate.—Freshly distilled anisole (470 g.) was heated under reflux and ethyl diazoacetate (100 g.) added dropwise during 4 hours. After 10—20 minutes a steady stream of nitrogen was evolved, and the mixture was heated for a further 2½ hours after the addition of all of the ethyl diazoacetate. The excess of anisole was removed at 100° under reduced pressure and the viscous dark brown oil distilled, yielding fractions: (i) b. p. up to 95°/0·4 mm. (6·5 g.), mainly anisole; (ii) b. p. 97—108°/0·4 mm. (60·9 g., 36% calc. on ethyl diazoacetate), a pale yellow oil giving a dark yellow colour with concentrated sulphuric acid; (iii) b. p. 132—150°/0·1 mm. (14 g.), a dark yellow oil giving a brown colour with sulphuric acid; and (iv) a residual brown tar (6·8 g.). Fraction (ii) was used in all of the following hydrolysis experiments.

4-*Methoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic Acid; Acid A.*—After potassium hydroxide (6·5 g.) in 95% ethanol (50 c.c.) had been shaken with fraction (ii) (10 g.) and kept for 15 minutes

at 0° the colourless potassium salt which had crystallised was separated and dried *in vacuo* (1·3 g.). The filtrate was heated at 100° for 1 hour (slight darkening), cooled, and acidified at 0—5° with 4N-hydrochloric acid (100 c.c.). Water (200 c.c.) was added, and the pale yellow precipitate of 4-*methoxy*cyclo*heptatrienecarboxylic acid* separated, washed with water, and dried under reduced pressure. The product (3·45 g.) was recrystallised several times from *cyclo*hexane, forming pale yellow leaflets, m. p. 143—144°. For analysis it was sublimed at 110°/0·05 mm. (Found: C 65·3; H, 5·9. $C_9H_{10}O_3$ requires C, 65·1; H, 6·1%). Light absorption in light petroleum (b. p. 40—60°): max. at 219 and 313 mμ; log ε 4·21 and 4·04 respectively; min. at 248 mμ; log ε 2·98. The infra-red spectrum of the acid as a mull in Nujol showed absorption maxima at 2631, 2525, 1666s, 1631, 1602s, 1536s, 1440s, 1408, 1335, 1290s, 1257s, 1219s, 1190, 1158s, 1136s, 1083, 1024s, 998, 950, 927, 918, 847, 815s, 788, 775, 765, 728s, and 673s cm.$^{-1}$ (s = strong absorption). The acid gave a yellow colour with concentrated sulphuric acid, reduced permanganate instantly in alkaline or acid solution, and rapidly decolorised a solution of bromine in chloroform.

4-*Ethoxy*-1 : 3 : 5-cyclo*heptatrienecarboxylic Acid; Acid B.*—(*a*) The ester mixture (5 g.) was hydrolysed as in the previous experiment with potassium hydroxide (3·25 g.) in 70% ethanol (30 c.c.). Any potassium salt which precipitated was not separated, and the mixture was heated on the steam-bath for 1 hour and acidified, without cooling, with 6N-hydrochloric acid (30 c.c.). The brown precipitate was separated, washed with water, and dried (220 mg.) over phosphorus pentoxide under reduced pressure. A further quantity (115 mg.) was obtained by dilution of the filtrate with water (10 c.c.) and keeping it at 0° overnight. The *ethoxy-acid* was obtained as colourless leaflets, m. p. 187—188°, by recrystallisation from benzene, and for analysis was sublimed at 150°/0·05 mm. (Found: C, 66·8; H, 6·5. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%). Light absorption in 95% ethanol; max. at 219 and 314 mμ; log ε 4·20 and 4·05 respectively; min. at 249 mμ; log ε 2·97. The infra-red spectrum of the acid as a mull in Nujol showed absorption maxima at 2631, 2518, 1666s, 1623, 1597s, 1526s, 1438s, 1420, 1402, 1366s, 1328, 1287s, 1259s, 1204s, 1166s, 1129s, 1108, 1083, 1034s, 1004, 961, 927, 908, 889, 841, 830, 808s, 763s, 734s, and 687s cm.$^{-1}$. The acid gave a yellow colour with concentrated sulphuric acid, instantly reduced permanganate, and rapidly decolorised bromine solutions.

(*b*) *From* 4-*methoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic acid.* Acid A, m. p. 144° (1 g.), was dissolved in ethanol (20 c.c.) containing sulphuric acid (3 drops), and the solution heated on the steam-bath for 30 minutes. Removal of most of the alcohol under reduced pressure caused the precipitation of a light brown solid which was crystallised from benzene, forming nearly colourless leaflets (753 mg.). After sublimation at 140°/0·05 mm. it gave colourless crystals, m. p. 186—188°, not depressed on admixture with acid B prepared by the foregoing method. No solid products were isolated from the mother-liquors.

Phenoxyacetic Acid.—The potassium salt (1 g.) obtained from the alkaline hydrolysis of the ester mixture (see preparation of acid A above) was suspended in ether (30 c.c.) and slowly acidified with concentrated hydrochloric acid (3 c.c.). The ethereal layer was removed, and the solid residue thoroughly extracted with ether (3 × 30 c.c.). The combined ethereal extracts were dried, and the solvent was removed, leaving a brownish residue (537 mg.) which was purified by sublimation at 80°/0·1 mm. and crystallisation from *cyclo*hexane; it formed colourless leaflets, m. p. 99° alone and mixed with an authentic specimen of phenoxyacetic acid (Found: C, 62·9; H, 5·3; OMe, 0·0. Calc. for $C_8H_8O_3$: C, 63·15; H, 5·3%). The product gave no colour with concentrated sulphuric acid, reduced alkaline permanganate slowly, and did not decolorise bromine in chloroform. The ultra-violet spectrum of a solution in 95% ethanol showed max. at 219, 264, 270, and 276 mμ; log ε 3·83, 3·05, 3·19, and 3·10 respectively (cf. Baly and Collie, *J.*, 1905, **87**, 1345). Infra-red spectrum (Nujol mull): max. at 2666, 2557, 1739s, 1703s, 1600s, 1584s, 1499, 1485, 1447s, 1307, 1293, 1283, 1261, 1226s, 1183, 1169, 1157, 1094s, 1071, 1021, 996, 961, 931, 913, 888, 835s, 822, 762, 755s, and 688s.

Ozonolysis of 4-*Methoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic Acid.*—A stream of ozonised oxygen (containing *ca.* 1% of ozone) was bubbled through a solution of Acid A (332 mg.) in ethyl acetate (25 c.c.) for 2 hours at 0°. The ozonide was decomposed by the addition of hydrogen peroxide (5 c.c. of 30%) and 2N-sodium hydroxide (12 c.c.), and the solution agitated for 2 hours. The aqueous layer was separated, acidified with concentrated hydrochloric acid (3 c.c.), and then extracted with ether (3 × 10 c.c.). After drying and removal of the solvent, the colourless crystals obtained (31 mg.) were recrystallised from water, to give needles, m. p. 183°, not depressed on admixture with an authentic specimen of anisic acid (Found: C, 63·2; H, 5·4. Calc. for $C_8H_8O_3$: C, 63·15; H, 5·3%).

Ozonolysis of 4-*Ethoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic Acid.*—As in the previous experi-

ment, acid B (332 mg.) in ethyl acetate (60 c.c.) was ozonised for 2 hours at 0°. Treatment as before gave an acid, m. p. 195°, as colourless leaflets after crystallisation from ethanol. The m. p. was not depressed on admixture with authentic *p*-ethoxybenzoic acid (Found: C, 65·3; H, 6·2. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·1%).

Hydrogenolysis of 4-*Methoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic Acid.*—Acid A (1 g.) in ethanol (100 c.c.) was hydrogenated at room temperature and pressure over Adams's platinum catalyst (25 mg.). After 32 hours the uptake of hydrogen (421 c.c. at N.T.P.) had ceased (405 c.c. required for 3 double bonds). The solvent was removed under reduced pressure, the yellow oily residue dissolved in ether, and the acidic fraction extracted into sodium hydrogen carbonate, and then after acidification back into ether. Removal of the solvent gave the hydrogenated acid as a dark yellow oil (633 mg.) which was distilled at 85°/0·01 mm., to give a pale yellow oil, which did not decolorise bromine or react with tetranitromethane. For identification it was converted into the acid chloride with thionyl chloride and then into the amide, colourless leaflets, m. p. 194° (corr.) (from water) (Found: C, 68·4; H, 10·6. Calc. for $C_8H_{15}ON$: C, 68·05; H, 10·7%). Willstätter (*Ber.*, 1898, **31**, 2504) gives m. p. 195° for *cyclo*heptanecarboxyamide.

Hydrogenation of 4-*Ethoxy*cyclo*hepta*-1 : 3 : 5-*trienecarboxylic Acid.*—Acid B (544 mg.) in ethanol (100 c.c.) was hydrogenated at room temperature and pressure over Adams's platinum catalyst (25 mg.). After 30 hours the absorption rate was negligible and the uptake of hydrogen (209 c.c. at N.T.P.) slightly less than that required (220 c.c.) for the saturation of 3 double bonds. The product was treated as in the foregoing experiment, and the acid fraction (540 mg.) distilled at 90° (bath-temp.)/0·01 mm., to yield a colourless oil which gave negative unsaturation tests. 4-*Ethoxy*cyclo*heptanecarboxyamide*, prepared as above, formed colourless leaflets, m. p. 127—128°, from water (Found: C, 65·4; H, 10·2. $C_{10}H_{19}O_2N$ requires C, 64·85; H, 10·35%).

4-*Keto*cyclo*heptatrienecarboxylic Acid.*—(*a*) Acid A (800 mg.) in chloroform (50 c.c.) was cooled in ice while bromine (0·27 c.c.) in chloroform (5 c.c.) was added during 10 minutes with frequent shaking. The solution darkened slightly and towards the end of the reaction a yellow oil separated which solidified when rubbed. The precipitate (600 mg.) was separated and formed a light grey powder after air-drying. Concentration of the filtrate under reduced pressure with subsequent cooling gave a further quantity (122 mg.) of the product which contained no bromine. Purification was achieved by crystallisation from ethyl acetate (300 c.c.) (charcoal), the acid being obtained as a colourless microcrystalline powder (221 mg.) which charred but did not melt at 235—240°. Larger crystals were obtained by crystallisation from nitrobenzene (Found: C, 64·3; H, 4·4. $C_8H_6O_3$ requires C, 64·0; H, 4·05%). The acid, which darkened in light, sublimed very slowly, only 5 mg. being obtained at 145°/2 × 10^{-5} mm. after 4 days. It was soluble in methanol or ethanol, insoluble in light petroleum, and sparingly soluble in ethyl acetate, ether, acetone, chloroform, or water, but formed a brownish-yellow solution in concentrated hydrochloric acid from which the free acid could be precipitated by dilution. Light absorption in 95% ethanol: max. at 233, 305, and 316 mμ; log ε 4·41, 3·84, and 3·84 respectively; min. at 259 and 311 mμ; log ε 3·19 and 3·83 respectively. The infra-red spectrum of the acid as a mull in Nujol showed absorption maxima at 1709s, 1628s, 1545s, 1422, 1328, 1265s, 1245, 1209s, 1086, 1025, 950, 903, 875s, 847s, 817, 772s, 755s, and 735s cm.$^{-1}$.

(*b*) Acid B (1 g.) in chloroform (50 c.c.) was treated at 0° with bromine (0·3 c.c.) in chloroform (2 c.c.) during 5 minutes. After 1 hour the precipitate (718 mg.) was separated and a further quantity (104 mg.) of the product obtained by concentration of the mother-liquors. The acid was purified by crystallisation from ethyl acetate as before and for analysis a small quantity was sublimed at 140°/5 × 10^{-4} mm. (Found: C, 63·9; H, 3·7%). The ultra-violet absorption spectrum of a solution in 95% ethanol showed maxima at 233, 305, and 315 mμ (log ε 4·41, 3·84, and 3·85 respectively), and minima at 262 and 311 mμ (log ε 3·25 and 3·83 respectively). Infra-red spectrum (Nujol mull): max. at 1709s, 1628s, 1545s, 1420, 1328, 1265s, 1245, 1210s, 1086, 1026, 950, 903, 875s, 848s, 817, 772s, 756s, and 735s cm.$^{-1}$.

Action of Alkaline Permanganate on 4-*Keto*cyclo*heptatrienecarboxylic Acid.*—A solution of this acid (900 mg.) in 95% ethanol (120 c.c.) was treated with a solution of potassium hydroxide (14 c.c. of 45%) and cooled to −5°. A cold solution of potassium permanganate (3·12 g.) in water (150 c.c.) was added dropwise during 80 minutes to the vigorously stirred solution of the potassium salt. The ethanol was then removed on the steam-bath under reduced pressure and the precipitated manganese dioxide separated and washed with a little hot water. The cooled filtrate was extracted with chloroform (6 × 100 c.c.) in order to remove neutral and basic components, and then acidified to pH 2 with 1 : 1 hydrochloric acid and thoroughly extracted with ether (12 × 100 c.c.). Removal of the solvent from the combined dried ethereal

extract gave a slightly tarry residue (206 mg.) which was extracted with hot dioxan. On cooling, the extract deposited a slightly yellow precipitate of terephthalic acid, which gave a colourless product after sublimation at 130°/5 × 10^{-4} mm. which did not melt below 360° (Found : C, 57·5; H, 4·1. Calc. for $C_8H_6O_4$: C, 57·8; H, 3·65%). This with ethereal diazomethane, gave the dimethyl ester, m. p. 139°, not depressed on admixture with authentic dimethyl terephthalate.

Alkaline Rearrangement of 4-*Keto*cyclo*heptatrienecarboxylic Acid.*—The acid (230 mg.) was added to a solution of potassium hydroxide (1 g.) in ethanol (80 c.c.) and water (20 c.c.), and the mixture which formed a dark red solution after 2 minutes became brownish-yellow on being kept overnight at room temperature. After 1 hour's heating on the steam-bath (no further colour change) the ethanol was removed under reduced pressure and the solid brown residue dissolved in ether and treated with diazomethane. Next day the solvent was removed, and the residue dissolved as far as possible in 4N-sodium carbonate solution and extracted with ether (3 × 50 c.c.). The solvent was removed from the combined ethereal extracts, and the solid residue sublimed at 120°/0·05 mm., to give colourless crystals (47 mg.) which crystallised from dilute methanol in long needles, m. p. 139·5—140°, undepressed on admixture with authentic dimethyl terephthalate (Found : C, 62·0; H, 5·3. Calc. for $C_{10}H_{10}O_4$: C, 61·85; H, 5·2%).

Grateful acknowledgment is made to Professor A. R. Todd, F.R.S., for his interest and encouragement and to several colleagues for helpful discussions. We thank the D.S.I.R. for a maintenance grant (to J. R. Bartels-Keith), and Dr. R. N. Haszeldine for spectral determinations.

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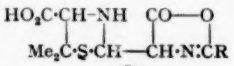
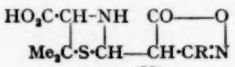
856. *Syntheses in the Penicillin Field. Part X.* 4-Formyl*isooxazolones *and Derived Thiazolidines.†*

By A. H. COOK and G. SHAW.

*iso*Oxazolones (IV) are difficultly accessible and their direct formylation seems impracticable. The formyl compounds (III) are, however, obtained by treating readily available benzylidene*iso*oxazolones (VII) with diphenylformamidine and hydrolysing the resulting anilinomethylene-*iso*oxazolones (VIII). The formyl compounds behave as aldehydes and yield thiazolidines.

WHEN penicillin was thought to possess the oxazolone-thiazolidine structure (I), synthesis of the analogous *iso*oxazolone-thiazolidines (II) was undertaken in the hope that these substances, in view of their spatial similarity to (I), might have useful antibacterial properties. The condensation of 4-formyl*iso*oxazolones (III) with penicillamine (ββ-dimethylcysteine) was accordingly investigated as a direct route to the required compounds.


(I)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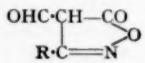
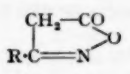

(III)

Initial experiments designed to prepare (III) involved formylation of 3-substituted *iso*oxazolones (IV) but a survey of the literature revealed that only one such authenticated compound (IV; R = Ph), prepared from ethyl benzoylacetate and hydroxylamine, was available (Dains and Griffin, *J. Amer. Chem. Soc.*, 1913, **35**, 959; Claisen and Zedel, *Ber.*, 1891, **24**, 140). Condensation of (IV; R = Ph) with ethyl formate and sodium, or with ethyl orthoformate and acetic anhydride, led in each case to the formation of a non-aldehydic yellow crystalline substance which must be the compound (V; R = Ph).

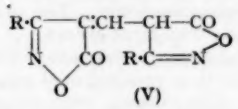
* Part IX, *J.*, 1950, 1947.

† Most of the work described in this paper was carried out during the war-time Anglo-American co-operative project on penicillin. None of the present work, however, is described in "The Chemistry of Penicillin," Princeton University Press, 1949.

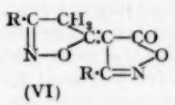
To ensure as close an approach as possible to the penicillin model it was desirable that the substituent R should be an alkyl or aralkyl group. A product of the reaction of ethyl acetoacetate and hydroxylamine (Hantzsch, *Ber.*, 1891, **24**, 498; Knorr and Reuter, *ibid.*, 1894, **27**, 1174; Wahl and Meyer, *Bull. Soc. chim.*, 1908, **3**, 952; Uhlenhuth, *Annalen*, 1897, **296**, 44) has been previously assigned the structure (IV; R = Me) but Donleavy



(IV)



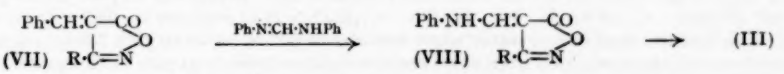
(V)



(VI)

and Gilbert (*J. Amer. Chem. Soc.*, 1937, **59**, 1072) have shown that the substance is in fact a bis-compound, probably (VI; R = Me). Moureau and Lezzenec (*Bull. Soc. chim.*, 1907, **1**, 1079) reported preparation of the ammonium salt of (IV; R = n-C_5H_{11}) from ethyl 3-keto-octanoate * and hydroxylamine in the presence of aqueous ammonia. This reaction was repeated and in addition a similar reaction was carried out with ethyl phenylacetoacetate and hydroxylamine, but in each case the compounds obtained appeared to be salts of (VI; R = n-C_5H_{11} and Ph·CH_2). The difficulties encountered in attempts to prepare (IV; R = n-C_5H_{11} and Ph·CH_2) and the failure of (IV; R = Ph) to undergo formylation by the usual procedures did not encourage further work along these lines, and attention was therefore turned to a survey of *iso*oxalones having a group in the 4-position capable of conversion into the formyl radical.

The most promising of such *iso*oxazolones appeared to be the anilinomethylene*iso*oxazolones (VIII) which were found to be readily obtainable in excellent yield by fusion of a mixture of the 4-benzylidene*iso*oxazolones (VII) with diphenylformamidine; the benzylidene derivatives were readily available from the reaction of benzaldehyde, hydroxylamine, and β-keto-esters (Dains and Griffin, *loc. cit.*). A few attempts were made to condense (VIII) with penicillamine and simple thiazolidines in the expectation that the desired analogues (II) would be obtained but these experiments were unsuccessful. It was soon found, however, that gentle hydrolysis of (VIII; R = Me, Ph, n-C_5H_{11}, and Ph·CH_2) with dilute (2%) sodium carbonate solution resulted in the liberation of aniline (cf. Ridi and Papini, *Gazzetta*, 1946, **76**, 376, who used potassium hydroxide), which was removed from the reaction mixture by distillation in steam, hydrolysis being deemed to be complete when the distillate failed to give a colour with sodium hypochlorite solution. When the ice-cold resulting solutions were acidified the formyl*iso*oxazolones (III; R = Me, Ph, n-C_5H_{11}, and Ph·CH_2) separated as crystalline solids. In addition small amounts of the bis-compounds (V) were isolated from the reaction mixtures except in the case (VIII; R = Me). It is noteworthy that more vigorous hydrolysis with N-sodium hydroxide gave the compounds (V) almost exclusively.



The formyl*iso*oxazolones, unlike the analogous hydroxymethyleneoxazolones, appeared to be true aldehydes as indicated by ready formation of 2 : 4-dinitrophenylhydrazones and reduction of ammoniacal silver nitrate. The aldehydes were also prone to self-condensation; thus a sample of (III; R = Ph) after being kept for three months was found to have been converted into (V; R = Ph), presumably with loss of formic acid. When the aldehydes (III; R = Me, Ph, n-C_5H_{11}, and Ph·CH_2) and penicillamine were brought together in ethanol or aqueous ethanol, the solutions soon failed to give ferric chloride and nitroprusside colour reactions of the thiol. From the solutions were isolated the required penicillin models (II; R = Me, Ph, n-C_5H_{11}, and Ph·CH_2) as pale yellow solids which could be precipitated from alkaline solution with acid; hydrolysis with warm dilute acid led to the re-formation of penicillamine and the formyl*iso*oxazolones. Assay of these *iso*oxazolone-thiazolidines (II) *in vitro* indicated that they were devoid of antibacterial activity.

* Geneva nomenclature, CO_2H = 1.

Experimental

The β-keto-esters employed were prepared by the Spassow method (Spassow, *Ber.*, 1937, **70**, 2381; Ogata *et al.*, *J. Pharm. Soc. Japan*, 1939, **59**, 105) by refluxing a mixture of ethyl acetoacetate, an acid chloride, and magnesium turnings in chloroform, followed by mild hydrolysis of the resultant diketo-ester with 2% aqueous ammonia. The yields were rarely greater than 50% but the method was less time-consuming than most others.

Reaction of Hydroxylamine with Ethyl Phenylacetoacetate.—The keto-ester (2 g.) and hydroxylamine hydrochloride (1 g.) were dissolved in concentrated aqueous ammonia (12 ml.), and the solution was set aside for 18 hours. The solvents were removed *in vacuo* over concentrated sulphuric acid, to leave a slightly sticky crystalline residue which, when triturated with dry ether, gave a colourless solid (0·4 g.). The solid separated from ethanol–benzene as needles, m. p. 185° (decomp.), and may be the *ammonium* salt of 3-benzyl-4-(3-benzyl*iso*oxazolin-5-ylidene)*iso*oxazol-5-one (VI; R = Ph·CH_2) (Found: C, 68·3; H, 5·5; N, 11·8. $C_{20}H_{20}O_3N_3$ requires C, 68·5; H, 5·7; N, 12·0%).

Reaction of 3-*Phenyl*iso*oxazol-5-one with Formylating Agents.*—The *iso*oxazolone (Dains and Griffin, *loc. cit.*; 1 g.), ethyl orthoformate (1 g.), and acetic anhydride (5 ml.) were warmed together on the steam-bath for 2 hours. The solvents were removed *in vacuo* and the resultant gum was dissolved in ethanol. Addition of water to the solution precipitated 4-(5-*keto*-3-*phenyl*iso*oxazolin*-4-*ylmethylene*)-3-*phenyl*iso*oxazol*-5-*one* (V; R = Ph) (0·8 g.) which separated from chloroform–light petroleum as yellow plates, m. p. 200° (Found: C, 68·6; H, 3·8; N, 8·3. $C_{19}H_{12}O_4N_2$ requires C, 68·7; H, 3·6; N, 8·4%). The same compound was obtained by treating 3-phenyl*iso*oxazol-5-one with ethyl formate and " molecular " sodium in benzene.

4-*Benzylidene- and* 4-*Anilinomethylene*-iso*oxazolones* (Dains and Griffin, *loc. cit.*).—The following compounds have not been described before: 3-*Benzyl*-4-*benzylidene*iso*oxazol*-5-*one* (VII; R = Ph·CH_2) separated from ethanol as pale yellow plates, m. p. 146—147° (Found: C, 77·2; H, 5·1; N, 5·3. $C_{17}H_{13}O_2N$ requires C, 77·5; H, 5·0; N, 5·3%). 4-*Anilinomethylene*-3-*benzyl*iso*oxazol*-5-*one* (VIII; R = Ph·CH_2) formed pale yellow plates (from benzene), m. p. 185—186° (decomp.) (Found: C, 73·6; H, 5·2; N, 9·8. $C_{17}H_{14}O_2N_2$ requires C, 73·4; H, 5·1; N, 10·0%). 3-n-*Amyl*-4-*benzylidene*iso*oxazol*-5-*one* (VII; R = *n*-C_5H_{11}) separated from ethanol as pale greenish-yellow sheaves, m. p. 76—77° (Found: C, 74·1; H, 7·1; N, 5·7. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·1; N, 5·8%). 3-n-*Amyl*-4-*anilinomethylene*iso*oxazol*-5-*one* (VIII; R = *n*-C_5H_{11}) formed yellow plates, m. p. 86—87°, from ethyl acetate–light petroleum (Found: C, 69·85; H, 7·2; N, 10·75. $C_{15}H_{18}O_2N_2$ requires C, 69·75; H, 7·0; N, 10·85%).

*Formyl*iso*oxazolones* (III).—The general method for the preparation of these substances is illustrated as follows: 4-Anilinomethylene-3-benzyl*iso*oxazol-5-one (12 g.) was treated with 2% sodium carbonate solution (250 ml.), and the mixture distilled in steam until a test portion of the distillate failed to give a purple colour with aqueous sodium hypochlorite, indicating the absence of aniline; this required 1—2 hours. Acidification of the pale yellow solution with hydrochloric acid and cooling gave 3-benzyl-4-formyl*iso*oxazol-5-one *monohydrate* (III; R = Ph·CH_2) (6 g.) which separated from ethyl acetate–light petroleum as pale yellow plates, m. p. 80° (Found: C, 59·8; H, 5·1; N, 6·3. $C_{11}H_9O_3N,H_2O$ requires C, 59·7; H, 5·0; N, 6·3%). The hydrate readily lost water when warmed to 60° *in vacuo* to give 3-*benzyl*-4-*formyl*iso*oxazol*-5-*one* which crystallised from ethyl acetate–light petroleum as pale yellow prisms, m. p. 112—113° (decomp.) (Found: C, 65·1; H, 4·5; N, 6·8. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·5; N, 6·9%). The 2:4-*dinitrophenylhydrazone*, prepared in aqueous-ethanolic sulphuric acid, crystallised from ethanol–water as yellow rosettes of needles, m. p. 150° (decomp.) (Found: C, 53·45; H, 3·5; N, 18·3. $C_{17}H_{13}O_6N_5$ requires C, 53·5; H, 3·4; N, 18·3%). Extraction of the filtrate from the above monohydrate preparation with chloroform (3 × 20 ml.) and evaporation of the solvent gave 3-*benzyl*-4-(3-*benzyl*-5-*keto*iso*oxazolin*-4-*ylmethylene*)iso*oxazol*-5-*one* (V; R = Ph·CH_2) (2 g.) which separated from chloroform–light petroleum as yellow plates, m. p. 154—155° (decomp.) (Found: C, 70·2; H, 4·7; N, 7·8. $C_{21}H_{16}O_4N_2$ requires C, 70·0; H, 4·5; N, 7·8%). The following substances were prepared in a similar manner: 4-*Formyl*-3-*phenyl*iso*oxazol*-5-*one monohydrate* formed pale brown needles (from ethyl acetate–light petroleum), m. p. 79—80° (Found: C, 58·0; H, 4·4; N, 6·65. $C_{10}H_9O_4N$ requires, C 58·0; H, 4·4; N, 6·8%); the anhydrous *aldehyde* (III; R = Ph), pale yellow prisms (from ethyl acetate–light petroleum), m. p. 178° (decomp. with darkening from 150°) (Found: C, 63·2; H, 3·9. $C_{10}H_7O_3N$ requires C, 63·45; H, 3·7%), gave a 2:4-*dinitrophenylhydrazone* which separated from dilute acetic acid as feathery orange needles, m. p. 167—168° (decomp.) (Found:

C, 51·6; H, 3·3; N, 18·7. $C_{16}H_{11}O_6N_5$ requires C, 52·0; H, 3·0; N, 19·0%). **3-*Phenyl*-4-(5-*keto*-3-*phenyl*isooxazolin-4-*yl*)*methylene*isooxazol-5-*one*** formed yellow plates (from chloroform–light petroleum), m. p. 200° (decomp.), identical with the compound obtained from 3-phenyl*iso*oxazol-5-one and formylating agents. **3-n-*Amyl*-4-*formyl*isooxazol-5-*one*** (III; R = n-C_5H_{11}) crystallised in pale yellow needles, m. p. 45°, from ethanol–water (Found: C, 58·9; H, 7·0; N, 7·4. $C_9H_{13}O_3N$ requires C, 59·0; H, 7·2; N, 7·65%); its **2 : 4-*dinitrophenylhydrazone*** formed scarlet needles, m. p. 135° (decomp.), from ethanol–water (Found: C, 49·4; H, 5·0; N, 19·2. $C_{15}H_{17}O_6N_5$ requires C, 49·6; H, 4·7; N, 19·3%). **3-n-*Amyl*-4-(3-n-*amyl*-5-*keto*isooxazolin-4-*ylmethylene*)isooxazol-5-*one*** (V; R = n-C_5H_{11}) crystallised in yellow needles (from ethyl acetate–light petroleum), m. p. 60° (Found: C, 63·8; H, 7·6. $C_{17}H_{24}O_4N_2$ requires C, 63·7; H, 7·6%). **4-*Formyl*-3-*methyl*isooxazol-5-*one*** (III; R = Me) separated as pale brown needles, m. p. 143—144° (decomp.), from ethyl acetate–light petroleum (Found: C, 47·4; H, 4·2; N, 11·05. $C_5H_5O_3N$ requires C, 47·3; H, 4·0; N, 11·05%); this compound was soluble in water but could be extracted therefrom with n-butanol. Its **2 : 4-*dinitrophenylhydrazone*** separated from methanol–acetic acid as scarlet prisms, m. p. 198° (decomp.) (Found: C, 43·1; H, 3·1; N, 22·75. $C_{11}H_9O_6N_5$ requires C, 43·0; H, 2·95; N, 22·8%).

*Reaction of the Formyl*isooxazolones *with Penicillamine.*—**2-(3-*Benzyl*-5-*keto*isooxazolin-4-*yl*)-5 : 5-*dimethylthiazolidine*-4-*carboxylic Acid*** (II; R = Ph·CH_2). 3-Benzyl-4-formyl*iso*oxazol-5-one (0·25 g.) and penicillamine hydrochloride (0·23 g.) were warmed in methanol (1·5 ml.) on the steam-bath for 2—3 minutes, after which a portion failed to give a blue colour with aqueous ferric chloride. The methanolic solution was added to water (10 ml.); the *thiazolidine* (0·3 g.) separated and was purified by dissolution in 2% sodium hydrogen carbonate solution, filtration, and precipitation with acid, to give a microcrystalline yellow powder, m. p. 163° (decomp.) (Found: C, 57·8; H, 5·25; N, 8·1. $C_{16}H_{18}O_4N_2S$ requires C, 57·5; H, 5·4; N, 8·4%). The thiazolidine (0·2 g.) was boiled with 2N-hydrochloric acid (2 ml.) for a short time; when cooled, the solution deposited 3-benzyl-4-formyl*iso*oxazol-5-one (0·05 g.), m. p. 80°, and the filtrate gave a deep blue colour with aqueous ferric chloride, typical of penicillamine. The following were prepared similarly: **2-(5-*Keto*-4-*methyl*isooxazolin-4-*yl*)-5 : 5-*dimethylthiazolidine*-4-*carboxylic acid*** (II; R = Me), a pale yellow powder, m. p. 170—171° (decomp.) (Found: C, 46·7; H, 5·7; N, 10·95. $C_{10}H_{14}O_4N_4S$ requires C, 46·5; H, 5·5; N, 10·85%). **2-(3-n-*Amyl*-5-*keto*isooxazolin-4-*yl*)-5 : 5-*dimethylthiazolidine*-4-*carboxylic acid*** (II; R = n-C_5H_{11}), a yellow powder, m. p. 141—142° (decomp.) (Found: C, 53·7; H, 7·0. $C_{14}H_{22}O_4N_2S$ requires C, 53·5; H, 7·05%). **2-(5-*Keto*-3-*phenyl*isooxazolin-4-*yl*)-5 : 5-*dimethylthiazolidine*-4-*carboxylic acid*** (II; R = Ph), a pale yellow powder, m. p. 124—125° (decomp.) (Found: C, 56·2; H, 5·1. $C_{15}H_{16}O_4N_2S$ requires C, 56·2; H, 5·0%).

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857. *The Potassium Thorium Fluorides.*

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Thermal analysis and microscopic examination have shown the following compounds to exist in the system $KF–ThF_4$: α-K_5ThF_9, β-K_5ThF_9, K_3ThF_7, α-K_2ThF_6, β-K_2ThF_6, $KThF_5$, KTh_2F_9, and KTh_3F_{13}. The compound α-K_5ThF_9 has not previously been described. The compound K_3ThF_7 is stable only at high temperatures and has been shown to disproportionate at lower temperatures into a mixture of β-K_2ThF_6 and β-K_5ThF_9. Discordant views in the literature as to the formula of the compound of highest thorium fluoride content have been discussed, and the formula KTh_3F_{13} for this compound confirmed. Partial solid solution has been shown to occur between KTh_3F_{13} and ThF_4. Optical properties have been recorded for the majority of the compounds listed.

Systematic precipitation studies in the systems $KF–Th(NO_3)_4–H_2O$ and $KNO_3–Th(NO_3)_4–HF–H_2O$ have shown that cationic complexes of thorium and fluorine strongly influence the composition of the precipitated potassium thorium fluorides. The hydrated compounds α-K_2ThF_6,nH_2O, KTh_2F_9,nH_2O, and ThF_4,nH_2O have been isolated from solution, but the compound $KThF_5$,nH_2O could not be isolated in a substantially pure state. Lattice water in the precipitated phases can be removed at 300° without appreciable loss of fluorine.

The preparation of hydrated potassium thorium fluorides approximating in composition to K_2ThF_6, $KThF_5$ (probably a mixture of K_2ThF_6 and KTh_2F_9), and KTh_2F_9 (Rosenheim, Samper and Davidsohn, *Z. anorg. Chem.*, 1903, **35**, 424) suggests a considerable degree of complexity for the binary system $KF–ThF_4$. Ample confirmation of this complexity was obtained from preliminary studies of the system and from the results of Dergunov and Bergman (*Doklady Acad. Nauk, S.S.R.*, 1948, **60**, 391) and Zachariasen (*J. Amer. Chem. Soc.*, 1948, **70**, 2147), published during the course of our investigations.

Dergunov and Bergman's thermal analysis suggested the existence, at least at high temperatures, of two compounds K_3ThF_7 and $KThF_5$ and indicated a formula KTh_3F_{13} for a congruently-melting compound appearing in the thorium-rich area of the system. No evidence was obtained for other compounds or for any polymorphic forms of the potassium thorium fluorides, nor was any evidence presented of solid solution between thorium fluoride and KTh_3F_{13}.

Zachariasen's *X*-ray examination, carried out on melts cooled to atmospheric temperature at different rates, revealed the existence of the compounds K_5ThF_9, α-K_2ThF_6, β-K_2ThF_6, $KThF_5$, and KTh_2F_9. The compound of highest ThF_4 : KF ratio was stated to be KTh_6F_{25}. No mention was made in this study of a compound of composition K_3ThF_7 or of any region of solid solution.

Since there are numerous discrepancies between the published results, a further study of the system $KF–ThF_4$ has been made by thermal analysis and by optical methods. Existence of an additional phase, α-K_5ThF_9, has been established. The compound K_3ThF_7 has been shown to disproportionate at approximately 570° into a mixture of β-K_5ThF_9 and β-K_2ThF_6. The composition of the phase in the thorium-rich portion of the system has been shown to be KTh_3F_{13}, rather than KTh_6F_{25}. This compound forms solid solutions with thorium fluoride containing up to 30% of KTh_3F_{13}. The only phases which could be precipitated in substantially pure state from aqueous solutions were hydrates of the compounds α-K_2ThF_6, KTh_2F_9, and ThF_4. Dehydration of these compounds without appreciable loss of fluorine could be completed by heating them for 3 hours at 300°, preferably in a current of inert gas.

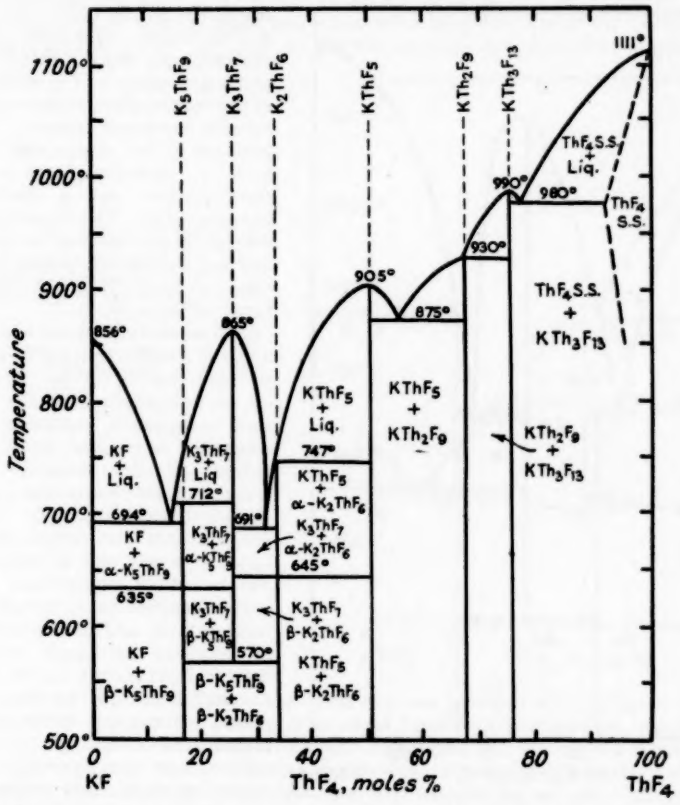
Experimental

Materials.—Hydrofluoric acid, thorium nitrate, ammonium fluoride, potassium nitrate, and reagents used for analysis were of analytical grade. Potassium fluoride was of reagent grade.

Preparation of Anhydrous Fluorides.—Two methods of preparation of anhydrous thorium fluoride were used. (*a*) Thorium nitrate (M/2) was added at 20° to a 10% excess of 30% hydro-

fluoric acid. All fluoride solutions were handled in polystyrene equipment. After 15 hours, the precipitate changed from a voluminous gel to a dense powder. This was centrifuged and washed five times by redispersion in water to remove nitrate. The product was dehydrated by heating it for 3 hours at 300° (see p. 4475). (*b*) Thorium oxide was heated for 3 hours at 200° with a two-fold excess of ammonium fluoride, a ' Monel ' vessel attached to a trap and vacuum system being used. Excess of ammonium fluoride was removed, and ammonium thorium fluoride was finally decomposed by heating the product *in vacuo* (<0·05 mm.) for 1 hour at 430°. Progress of fluorination of thoria was followed by testing the solubility of the mixture in boiling 15% solutions of the tetrasodium salt of ethylenediaminetetra-acetic acid. Blank tests showed

FIG. 1. *The system* $KF–ThF_4$.



that this reagent did not dissolve unchanged thorium oxide. Products completely soluble in the reagent were obtained.

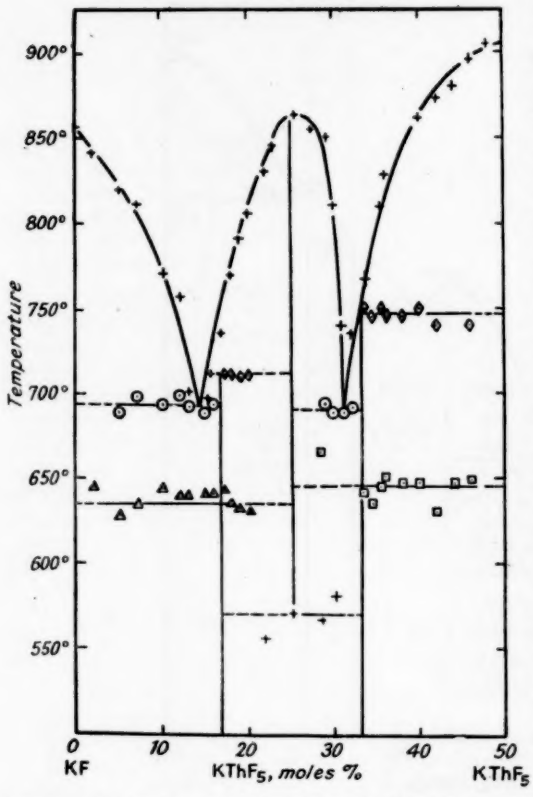
Traces of nitrate (0·005—0·01 mol.) and of ammonia (0·004—0·02 mol.) were detected in products made by methods (*a*) and (*b*), respectively. The atomic ratio of fluorine to thorium in precipitated thorium fluoride agreed with the theoretical value but fell to 3·96—3·97 after dehydration of the fluoride at 300°. Unless dehydration was complete, a further small loss of fluorine occurred on fusion of the product in argon. Since the bulk of the thorium fluoride used in the study of the system $KThF_5–ThF_4$ was prepared by this method, it was assumed that the product contained approximately 1% of oxyfluoride or oxide impurities, although neither of these compounds of high refractive index could be detected under the microscope. The effect of this quantity of oxyfluoride or oxide impurity on the m. p. of pure thorium fluoride was not investigated, but the effect was presumed to be small and to vanish at the composition $KThF_5$. Later work on thorium fluoride, including the determination of its m. p., was carried out with

material made by method (*b*). The atomic ratio of fluorine to thorium in this product agreed with the theoretical value and was not changed by fusion of the product in argon.

A double fluoride served as a convenient source of material for work in the system KF–$KThF_5$. It was prepared by adding M-potassium fluoride (5 mol.) to 0·2M-thorium nitrate (1 mol.) and treating the precipitate as described for thorium fluoride. The composition of the product, after drying at 300°, was $K_{1\cdot05}ThF_{5\cdot01}$. Loss of fluorine from this product on drying or fusion was negligible.

Phase Analysis of the System KF–ThF_4.—(a) *Thermal analysis.* To maintain an atmosphere of argon over the charge, a crucible drilled from a length of " Monel " metal rod was placed in a vertical, close-fitting " Monel " tube which was sealed at its lower end. The upper end of this tube accommodated a " Sindanyo " plug with orifices for thermocouple leads, " Monel " stirrer, and argon supply. The major portion of the tube was heated in a well-lagged, tubular resistance furnace. The temperature of the charge was measured with a platinum–platinum-rhodium thermocouple and a thermocouple potentiometer. The thermocouple was frequently calibrated at the silver, zinc, and sodium chloride points, and at no time was found to be in error by more than $+3°$ or $-2°$.

FIG. 2. *The system* KF–$KThF_5$.



All melts were stirred while cooling and the solidified products were used to obtain heating curves. With cooling curves, temperatures at the m. p.s of pure compounds, eutectics, and incongruent m. p.s were reproducible to within $\pm3°$, but transition temperatures of solid compounds were reproducible to within only $\pm5°$. Liquidus temperatures were often difficult to locate precisely and in general could not be easily reproduced. Heating curves enabled us to obtain eutectic temperatures and incongruent m. p.s in excellent agreement with those derived from cooling curves, but were unsatisfactory for locating liquidus points. Transition temperatures obtained from heating curves were higher than corresponding temperatures obtained from cooling curves by 10—20° for the α–β transition of K_5ThF_9 and by 30—40° for the α–β transition of K_2ThF_6.

Where incongruent or near-incongruent melting systems were found, it was noted that arrests appeared at unexpected positions on the cooling curves, *e.g.*, at temperatures corresponding to eutectics or incongruent m. p.s of adjacent compounds (Figs. 2 and 3). This behaviour was attributed to incomplete establishment of equilibrium between the liquid and interacting solid during the cooling period.

After fusion, the composition of mixtures was checked by analysis at a number of points on the phase diagram. No significant departure from the calculated compositions was detected.

For the study of certain lower-temperature transitions a method of differential thermal analysis was used. The furnace and nickel sample block were as described by Berkelhamer (Tech. Paper 664, 1945, U.S. Bur. Mines). The sample (0·45 g.) was heated at a uniform rate of 8° per min., calcined alumina being used as a reference material. The output of the platinum–platinum-rhodium differential thermocouple was amplified and recorded on a strip chart poten-

tiometer responsive to rapid changes in applied voltage. High amplification of the differential temperature was necessary to obtain a clear record of the thermal changes of the substance K_3ThF_7.

(b) *Analysis by optical examination of quenched melts.* This technique (Rankin and Wright, *Amer. J. Sci.*, 1915, **39**, 1; Faust, *Amer. Min.*, 1936, **21**, 735) is of particular value in the study of systems subject to a high degree of supercooling, and it has been employed in the study of the system KF–ThF_4 where the thorium fluoride content of the melts exceeded 70 moles %. In these melts the degree of supercooling of the liquidus, even with vigorous stirring, was so large (of the order of 100° with pure thorium fluoride) that location of liquidus points by thermal analysis alone became impossible.

The equipment consisted of a vertical alumina tube furnace, a thermocouple and potentiometer for temperature measurement, and a controller of special design for maintaining furnace temperatures within ±0·5°. A holder for the thermocouple and lead-in wires adequately sealed

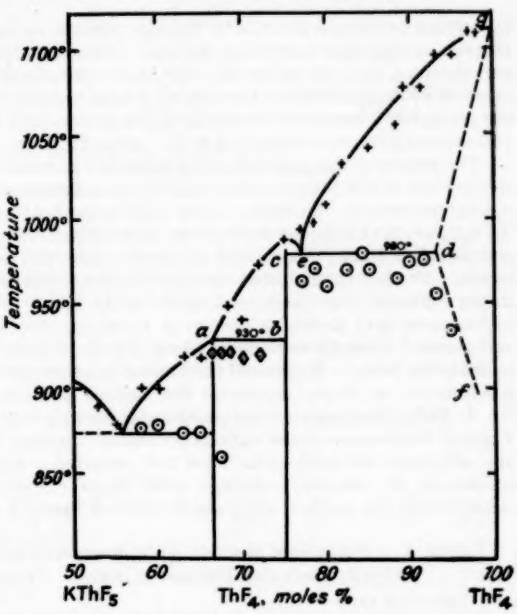


FIG. 3. *The system* $KThF_5$–ThF_4.

(Liquidus curves at ThF_4 concentrations exceeding 70 moles % obtained from quenching experiments. Position of eutectic lines *ab* and *cd* in accordance with quenching data shown 10—15° above points obtained from cooling curves.)

the upper end of the furnace tube. The lower end was provided with a stopper carrying a tube for admission of oxygen-free argon. The usual procedure consisted in wrapping a sample weighing several mg. in thin platinum foil and suspending the foil by thin (0·002 in.) platinum wire from heavier-gauge platinum leads through which current from a battery could be passed. The hot junction of the thermocouple was close to the suspended sample. After the charge had been kept for a suitable time at the required temperature the lower end of the furnace tube was opened, and the battery switch was closed to fuse the suspension and drop the charge into a bath of cold water. In the system KF–ThF_4 liquids did not quench to glasses but to crypto-crystalline material which was readily distinguishable from the larger and usually better-formed crystals that represented the solid phase in the system solid + liquid. Macrocrystalline phases present in the quenched specimens were distinguished by optical microscopy.

The results of the thermal and quenching studies are presented as a phase diagram of the system in Figs. 1, 2, and 3. Optical properties of various compounds are summarised in Table 1, which also compares densities determined in pure benzene with values calculated by Zachariasen. The density and optical properties of α-K_5ThF_9 and K_3ThF_7 could not be determined, as α-K_5ThF_9 reverted to the β-form when quenched, while K_3ThF_7 disproportionated into other compounds.

Precipitation of Potassium Thorium Fluorides from Aqueous Solution.—A systematic study of the precipitated phases was made. The sparingly soluble binary fluorides were obtained at 20°

TABLE 1. *Optical properties of anhydrous potassium thorium fluorides.*

Phase	Crystal system *	α or ε	γ or ω	D.R.	2V	Sign	ρ_{25} This investigation	ρ_{25} Zachariasen
ThF_4	Monoclinic	1·494	1·526	0·032	64°	+ve	6·29	6·14 †
KTh_2F_{13}...	Hexagonal	1·519	1·536	0·017	Uniaxial	−ve	6·23	—
KTh_2F_9 ...	Orthorhombic	1·490	1·532	0·042	16°	−ve	6·09	6·04
$KThF_5$ ...	Rhombohedral	1·470	1·475	0·005	Uniaxial	−ve	5·23	5·10
β-K_2ThF_6	Hexagonal	1·488	1·463	0·025	Uniaxial	+ve	4·82	4·91
α-K_2ThF_6	Cubic	1·45(5) ‡	—	—	—	—	—	4·33
β-K_5ThF_9	Orthorhombic	1·397	1·403	0·006	High	−ve	3·60	3·58
KF	Cubic	1·352	—	—	—	—	2·50	2·54 †

* Except for KF after Zachariasen (*loc. cit.*) and MDDC–1151, 1947. † Calc. from *X*-ray data.
‡ Determined on precipitated material dried at 300°.

by adding potassium fluoride to thorium nitrate, or by adding hydrofluoric acid to mixtures of thorium nitrate and potassium nitrate. Fluoride added was equivalent to the total potassium and thorium, and, except in the first four experiments in Table 3, sufficed to complete precipitation of M/30-quantities of thorium in a total volume of 250—300 ml. Unless stated otherwise, the precipitant was added dropwise in the above order in approximately 4 minutes. In general, voluminous gels were formed at first. After 15 hours these became dense and powdery.

The results of the precipitation studies are presented in Tables 2 and 3. The minute state of subdivision of the binary compounds (1—3 microns) precluded adequate determination of their optical properties. However, under high magnification (×980) aggregated products containing KTh_2F_9 or $KThF_5$ were seen to be anisotropic. Products containing as a major phase the compound α-K_2ThF_6 consisted of larger, spherical aggregates which were substantially isotropic. Freshly precipitated thorium fluoride gels dried in air consisted of amorphous, isotropic material, but specimens aged for 15 hours or more in solutions containing excess of hydrofluoric acid showed a fibrous or fascicular structure. The fibres, which were anisotropic and showed straight extinction along the fibre axis, served to identify aged samples of the hydrated fluoride. Because of the limited information obtainable from optical observation of the precipitates, an *X*-ray report on the various potassium thorium fluorides was obtained from Dr. A. McL. Mathieson. The powder data were obtained with nickel-filtered copper radiation. The cell dimensions of the various potassium thorium fluorides have been given by Zachariasen (*loc. cit.*) but intensity data were not reported. Identification was therefore based on the agreement of observed spacings with those calculated from the cell dimensions. Phases identified by this method are given in col. 3 of Tables 2 and 3.

TABLE 2. *Potassium thorium fluorides precipitated by hydrofluoric acid from mixtures of potassium and thorium nitrates. Products dried for* 15 *hr. at* 110°.

Molecular ratio: KNO_3	$Th(NO_3)_4$	HF	Composition of product	Phases identified by *X*-ray examination: major	minor
110	1	114	$K_{1\cdot15}ThF_{5\cdot18}$,0·28$H_2O$	α-K_2ThF_6	KTh_2F_9
50	1	54	$KTh_{0\cdot996}F_{5\cdot14}$,0·27$H_2O$	α-K_2ThF_6	KTh_2F_9
20	1	24	$KTh_{1\cdot25}F_{6\cdot10}$,0·45$H_2O$	α-KTh_2F_9	α-K_2ThF_6
10	1	14	$KTh_{1\cdot61}F_{7\cdot46}$,0·70$H_2O$	KTh_2F_9	—
5	1	9	$KTh_{1\cdot75}F_{8\cdot04}$,0·89$H_2O$	KTh_2F_9	—
2	1	6 (*a*)	$KTh_{2\cdot01}F_{8\cdot81}$,0·88$H_2O$	KTh_2F_9	—
—	—	— (*b*)	$KTh_{1\cdot92}F_{8\cdot69}$,1·60$H_2O$	KTh_2F_9	—
1	1	5	$KTh_{2\cdot00}F_{8\cdot90}$,0·87$H_2O$	KTh_2F_9	—
1	2	9 (*c*)	$KTh_{2\cdot75}F_{12\cdot0}$,2·68$H_2O$	KTh_2F_9	(ThF_4,*n*H_2O) *
—	—	— (*d*)	$KTh_{3\cdot32}F_{14\cdot1}$,2·54$H_2O$	KTh_2F_9	(ThF_4,*n*H_2O) *
1	5	21	Gel obtained only	—	—
1	10	41	$K_{0\cdot071}ThF_{4\cdot06}$,0·90$H_2O$	(ThF_4,*n*H_2O) *	KTh_2F_9

(*a*) $Th(NO_3)_4$ added to KNO_3 + HF. (*b*) Same order of precipitation as in (*a*); air-dried at 20°. (*c*) Air-dried. (*d*) Washed with 0·1N-HNO_3, then water, and air-dried.
* Phase not identified by *X*-ray examination; presence of ThF_4 deduced from analysis and/or microscopic examination.

Examination of anhydrous thorium fluoride showed products obtained by dehydration of the precipitated fluoride, or by fluorination of thorium oxide with ammonium fluoride, to be identical. Gelatinous thorium fluoride gave no powder pattern, but the fibrous hydrate, containing 2—3 moles of water, gave a pattern with a long spacing of 17 Å which could not be identified.

Dehydration of Hydrated Fluorides.—A small platinum boat containing the fluoride was placed in a platinum tube and heated in a current of dry air. Both the loss in weight of the fluoride and the hydrofluoric acid evolved on heating were determined, the acid vapours being conducted through polythene tubing into dilute sodium hydroxide. Fluorine was then determined by titration with thorium nitrate. Trial experiments using 7 mg. quantities of pure hydrofluoric acid gave fluorine recoveries of not less than 97%. The composition of the samples used

TABLE 3. *Potassium thorium fluorides precipitated by potassium fluoride from thorium nitrate. Products dried for* 15 *hr. at* 110°.

Molecular ratio: KF : $Th(NO_3)_4$	Composition of product	Phases identified by *X*-ray examination: major	minor
0·3	No precipitate	—	—
1·0	No precipitate	—	—
1·5	Opalescence only	—	—
3·0 †	$K_{0\cdot93}ThF_{3\cdot99}.2\cdot22H_2O$	(ThF_4,nH_2O)*	—
4·0	$KTh_{2\cdot38}F_{10\cdot5}.0\cdot98H_2O$	KTh_2F_9	—
5·0	$KTh_{0\cdot99}F_{4\cdot87}.0\cdot43H_2O$	α-K_2ThF_6 ‡	(KTh_2F_9) *
10·0	$K_{1\cdot27}ThF_{5\cdot19}.0\cdot29H_2O$	α-K_2ThF_6	—
20·0 (*a*)	$K_{1\cdot45}ThF_{5\cdot53}.0\cdot53H_2O$	α-K_2ThF_6	KTh_2F_9 + $KThF_5$
— (*b*)	$K_{1\cdot59}ThF_{5\cdot59}.0\cdot59H_2O$	α-K_2ThF_6	$KThF_5$
40·0 (*c*)	$K_{1\cdot59}ThF_{5\cdot57}.0\cdot25H_2O$	α-K_2ThF_6	—

(*a*, *b*, *c*) $Th(NO_3)_4$ added to KF : (*a*) rapidly (0·5 min.), (*b*) slowly (2 hr.).
* See Table 2, footnote (*). † Precipitation incomplete.
‡ On a second occasion KTh_2F_9 was identified as major phase.

was approximately as follows, only the fluorine and water contents being known exactly : (I) $KThF_5,nH_2O$ (25·0%F), (II) KTh_2F_9,nH_2O (24·5% F), and (III) ThF_4,nH_2O (20·5% F). Water in these samples was determined by igniting them with litharge and weighing the water evolved. Samples were first dried in air, (I) and (II) at 105° and (III) at 20°. Table 4 shows the results obtained.

Analytical Methods.—All samples prepared by precipitation were decomposed by fuming in platinum dishes with concentrated sulphuric acid. The bulk of the excess of acid was finally

TABLE 4. *Loss of water and hydrogen fluoride from hydrated fluorides on heating.*

Sample	Temp.	Time, hr.	Wt. loss, %	F loss, % of total F	Sample	Temp.	Time, hr.	Wt. loss, %	F loss, % of total F
* $KThF_5,nH_2O$	300°	1	2·37	nil	† KTh_2F_9,nH_2O	300°	2	2·72	0·12
	,,	2	2·52	0·008		400	2	3·02	0·46
	,,	4	2·59	0·024					
	400	1	2·64	0·096	‡ ThF_4,nH_2O ...	300	2	15·3	0·16
	,,	2	2·60	0·16		,,	4	15·5	0·30
	,,	4	2·64	0·17					

H_2O, determined by litharge method : * 2·47, † 3·09, ‡ 15·5%.

volatilised. All samples prepared by fusion required heating with ammonium fluoride before fuming with sulphuric acid and ammonium sulphate.

(i) Thorium in the clear aqueous extracts was precipitated by slow addition of 10% oxalic acid solution at 80°. The oxalate was then ignited to oxide and weighed. Results accurate to within 1—2 parts in 750 were obtained by this procedure.

(ii) Potassium in the thorium-free filtrate was determined as the sulphate after excess of oxalic acid had been destroyed by fuming with sulphuric acid. Residual ammonium sulphate was volatilised at 750° Negligible loss of potassium occurred through co-precipitation with thorium oxalate.

(iii) Water was at first determined by heating the various fluorides with ignited litharge and collecting the water evolved. All later determinations were made by measuring the loss in weight of the fluorides after 3 hours at 300°.

(iv) Residual nitrate in the precipitated fluorides was reduced with Devarda's alloy and determined as ammonia.

(v) Fluorine in the binary fluorides was determined by Willard and Winter's procedure, 50% sulphuric acid being used to volatilise fluorosilicic acid. Fused samples were given a preliminary fusion with sodium hydroxide. Reagent-grade sodium fluoride used as a titrimetric standard was analysed by conversion into sodium sulphate and by heating to constant weight at

750°. It was found to contain 99·2% of sodium fluoride and 0·70% of water. The reliability of the distillation and titration techniques for fluorine was checked with a U.S. Bureau of Standards analysed sample of fluorspar, which was distilled with perchloric acid, and a sample of Greenland cryolite, which was distilled with sulphuric acid. Results in agreement with the calculated fluorine contents of these samples were obtained.

Use of perchloric acid for distillation of fluorine from thorium fluoride caused recovery of only 60—80% of the fluorine recoverable by distillation, under similar conditions, with sulphuric acid. Preliminary fusion with sodium hydroxide did not increase the fluorine recovery. It is presumed that complexes between thorium and fluoride ions (see p. 4479) hinder volatilisation of fluorosilicic acid, absence of the effect with sulphuric acid probably resulting from precipitation of sparingly soluble hydrates of thorium sulphate during the distillation process.

Fluorine in pure thorium fluoride was checked by two independent methods of analysis since the stoicheiometric ratio of fluorine to thorium was never attained in products analysed by Willard and Winter's procedure. Usually this ratio was in the range 3·95—3·99. Fischer and Peisker's method (*Z. anal. Chem.*, 1933, **95**, 225) gave results in good agreement with those obtained by Willard and Winter's procedure. Allowance was made for the increased solubility of lead chlorofluoride in sodium nitrate, derived from the fusion mixture used to decompose the sample. Warf's method (" The Analytical Chemistry of the Manhattan Project," edited by C. J. Rodden, p. 729, McGraw-Hill, New York, 1950), involving pyrohydrolysis of thorium fluoride at 1000° in a current of steam in a platinum tube and simple titration of hydrofluoric acid in the condensate, gave ratios of fluorine to thorium virtually identical with the theoretical value. Care was needed, however, to prevent carry-over of solid products into the condensate. Allowance was made for nitric acid volatilised from thorium fluoride containing nitrate impurities. It was concluded that classical methods of fluorine analysis are subject to error when applied to pure thorium fluoride, giving results approximately 1·5% low even if all precautions have been taken. For this reason Warf's method was finally adopted for analysis of thorium fluoride. It has the advantage that the thorium content of the sample can be simply determined by weighing residual thorium oxide.

Discussion

(i) *Thermal Analysis of the System* KF–ThF_4.—Six compounds have been shown to exist in the system KF–ThF_4 (Fig. 1), *viz.*, the congruently melting compounds K_3ThF_7, K_2ThF_6, $KThF_5$, KTh_2F_9, and KTh_3F_{13}, and the incongruently melting compound K_5ThF_9.

The sub-system KF–K_5ThF_9. Pure potassium fluoride synthesised from analytical-grade reagents melted at 856° ± 2°, in agreement with Bergman and Dergunov (*Doklady Acad. Nauk. S.S.R.*, 1941, **53**, 753). The reagent-grade product melted at 852°. The melting point is lowered rapidly by addition of thorium fluoride until the eutectic composition is reached at 694° (14 moles % of thorium fluoride). The compound K_5ThF_9 was found to be dimorphic, the high-temperature or α-form melting incongruently at 712° and changing sharply at 635° into a low-temperature form. The compound described by Zachariasen is therefore the β-phase. The experimentally determined density of β-K_5ThF_9 agrees satisfactorily with the value calculated from the cell constants (Table 1). β-K_5ThF_9 is hygroscopic and is decomposed by water.

The sub-system K_5ThF_9–K_3ThF_7–K_2ThF_6. Addition of thorium fluoride to K_5ThF_9 raises the liquidus of the system to a clearly defined maximum at 865° (25 moles % of thorium fluoride), thus confirming the peak found by Bergman and Dergunov (25 moles %, 870°) and establishing the existence, at higher temperatures, of the compound K_3ThF_7. Further addition of thorium lowers the liquidus of the system to a eutectic at 691° (31 moles % of thorium fluoride) between K_3ThF_7 and α-K_2ThF_6.

Weak arrests on the heating curves of mixtures containing approximately 25 moles % of thorium fluoride suggested a thermal change in the compound K_3ThF_7 at approximately 590°. Unequivocal evidence for this change was obtained from a differential thermal analysis of a previously fused mixture of the stoicheiometric composition. A sharp endothermic peak rising from 570° to a maximum at 600° was obtained on the heating curve, and a broader, exothermic peak rising from 575° to a maximum at 545° appeared on the cooling curve. The areas of these peaks were approximately equal. Weaker

thermal effects were obtained at approximately these temperatures with mixtures within the ranges of composition 16·6—25 and 25—33·3 moles % of thorium fluoride, respectively, but no thermal effects below 600° were detected at the compositions K_5ThF_9 or K_2ThF_6. When the solid reaction product of overall composition K_3ThF_7 was kept at 700° for 20 hours and then rapidly quenched, *X*-ray powder photographs showed the presence of β-K_5ThF_9. Lines corresponding to this latter phase were broad in the high sin θ region. Also shown on the photographs were lines, very sharp up to the limit of sin θ, which presumably correspond to the phase K_3ThF_7. It was impossible to differentiate lines corresponding to K_3ThF_7 from those of β-K_5ThF_9 in the low-angle region, and hence impossible to determine the crystal structure of this phase. If the quenched sample was rephotographed several days later the pattern of β-K_5ThF_9 was found to have faded and the dominating pattern was that of β-K_2ThF_6 with, however, an expanded unit cell, $a = 6{\cdot}645$ and $c = 3{\cdot}845$ Å, compared with the normal cell dimensions 6·571 and 3·817 Å, respectively. Evidently the phase K_3ThF_7 disproportionates at approximately 570°: $3K_3ThF_7 \longrightarrow$ β-$K_5ThF_9 + 2$β-K_2ThF_6. Initially, the mixture of disproportionation products contains residual K_3ThF_7, large crystals of which give the very sharp diffraction lines. It is possible that transition from K_3ThF_7 to β-K_5ThF_9 is relatively easy compared with that from K_3ThF_7 to β-K_2ThF_6, since the bulk of the initially formed mixture appears to consist of smaller crystals of β-K_5ThF_9 and particles of the expanded form of β-K_2ThF_6 which are less than 100 Å in diameter. After several days, when disproportionation is complete, the expanded form of β-K_2ThF_6 increases in particle size until this substance dominates the diffraction pattern.

The density of the reaction products ($\rho_{25} = 4{\cdot}03$) agrees satisfactorily with that calculated for complete disproportionation of K_3ThF_7. The optical properties of these products are, however, anomalous. Thus the mixture containing 25% of thorium fluoride is apparently homogeneous under the microscope. The birefringence of the quenched mixture is very low, the product resembling a compound with refractive indices $\alpha = 1{\cdot}410$ and $\gamma = 1{\cdot}412$. It is presumed that the minute crystal size of both β-K_5ThF_9 and β-K_2ThF_6 causes the mixture to simulate an isotropic compound. If, however, the products are heated for at least 30 hours at 500° in an inert atmosphere and then cooled, crystal growth occurs and the apparently homogeneous mixture breaks up into its visibly anisotropic components. The area of the differential temperature peak at the disproportionation temperature suggests that the heat evolved in the above reaction is approximately 6 kcal. per mole of K_3ThF_7.

The compound K_2ThF_6 is the second of its type in the system KF–ThF_4 to exist in polymorphic forms. The α-phase melts at 747° and on cooling reverts sharply at 645° to the β-form. The density of cold melts containing 33 moles % of thorium fluoride was in approximate agreement with the value calculated by Zachariasen for β-K_2ThF_6. Attempts to obtain the α-phase by quenching at precisely the stoicheiometric composition were unsuccessful, but samples quenched from near this composition gave sufficient of the α-phase for optical examination. A disordered form of β-K_2ThF_6 has been reported by Zachariasen but no thermal effect ascribable to an order–disorder transition in β-K_2ThF_6 was detectable by differential thermal analysis.

The sub-system K_2ThF_6–KTh_2F_9. A well-defined maximum on the liquidus of this system at 905° denotes the compound $KThF_5$. A simple eutectic between $KThF_5$ and KTh_2F_9 is formed at 875° (56 moles % of thorium fluoride). The compound KTh_2F_9 is just able to melt congruently at 930°. Neither $KThF_5$ nor KTh_2F_9 shows evidence of polymorphism.

The sub-system KTh_2F_9–ThF_4. Bergman and Dergunov, and also Zachariasen, both report a compound between thorium fluoride and the composition 66 moles % of thorium fluoride, the former claiming its composition to be KTh_3F_{13} and the latter to be KTh_6F_{25}. The composition KTh_6F_{25} does not explain the results of the quenching experiments. Because of the determined liquidus a compound KTh_6F_{25} should have an incongruent melting point and be stable below the line *cd* (Fig. 3), the approximate position of which has been verified by quenching experiments and by cooling curves. However, charges of the composition KTh_6F_{25} held for periods of 1—2 hours at temperatures below the line *cd*

showed no trace of fusion and consisted of a mixture of the monoclinic solid solution of thorium fluoride and a hexagonal phase. The hexagonal phase therefore cannot have the composition KTh_6F_{25}. Quenched charges of compositions containing 78·5 moles % or more of ThF_4 contained this compound as a primary phase. In quenches containing 77 moles % or less of ThF_4, the primary phase was a uniaxial compound which frequently exhibited well-developed hexagonal cross-sections under the microscope. The presence of these crystals above the line *cd* indicated a congruent m. p. for this compound. The position of the eutectic *e* (980°, 78 moles % of ThF_4) was determined from the position of the line *cd* and the change in primary phase between 77 and 78·5 moles % of ThF_4. The quenching data gave figures 10—15° higher than did the cooling curves for the eutectic lines *ab* and *cd*. The data therefore indicate that the hexagonal crystals were of the composition KTh_3F_{13} reported by Bergman and Dergunov. This compound, however, was found to melt at 990°, some 20° above the value found by them. Solid solution between KTh_3F_{13} and thorium fluoride is shown by the increasingly small interval between solidus and liquidus in the range of compositions 93—100 moles % of thorium fluoride, and by the presence of a uniphase solid at all points in the area *fdg*. Only in the area *bcdf* does the hexagonal phase appear with the solid solution phase. The extent of solid solution of the compound KTh_3F_{13} in thorium fluoride was not accurately determined but was of the order of 30%. No evidence for solid solution in this system has been presented by other investigators.

Pure thorium fluoride was found to melt at 1111° ± 2°: Bergman and Dergunov give 1114°. Fusion of thorium fluoride in the quenching furnace readily caused formation of the oxyfluoride, $ThOF_2$, or the oxide unless all traces of moisture and oxygen were excluded. Almost complete conversion into these highly refractive phases occurred if the fluoride was heated in air in an open crucible. Thorium oxide was the final product. Compositions containing potassium fluoride appeared to absorb oxygen less readily, particularly below 90 moles % of thorium fluoride. The structures of both thorium fluoride and thorium oxyfluoride have been determined by Zachariasen (*Acta Cryst.*, 1949, **2**, 388).

(ii) *Isolation of Potassium Thorium Fluorides from Aqueous Solutions.*—Precipitation studies in the systems $KF–Th(NO_3)_4–H_2O$ and $KNO_3–Th(NO_3)_4–HF–H_2O$ reveal a complicated behaviour attributable to complex formation between thorium and fluoride ions. Dodgen and Rollefson (*J. Amer. Chem. Soc.*, 1949, **71**, 2600) have shown that the ionic species in acid solutions containing thorium and fluoride ions are ThF^{3+}, ThF_2^{2+}, and ThF_3^{1+}, the ion ThF_2^{2+} being the dominant ion at the point of precipitation of hydrated thorium fluoride. Day and Stoughton, however (A. E.C.D. 2756, 1949), found more probable formulæ for the complex ions to be $ThF(NO)_3^{2+}$ and $ThF_2(NO_3)^{1+}$. Whichever formulation of the complex ions is most appropriate, it is clear that association of fluoride ion with thorium so alters the fluoride-ion concentration that mixing of given molar proportions of potassium, thorium, and fluoride ions results in the precipitation of a binary fluoride differing markedly from the expected composition (cf. Tables 2 and 3).

Thorium fluoride, in addition to the compounds α-K_2ThF_6, $KThF_5$, and KTh_2F_9 isolated by earlier workers, has been isolated from solution. All other phases were decomposed by water to more stable substances. In the majority of cases mixtures of two or more phases were obtained, phases approximating in composition to $KThF_5$, for example, often consisting of KTh_2F_9 and α-K_2ThF_6 in approximately equal proportion. In general, solutions of low potassium fluoride, or low potassium fluoride plus nitric acid concentration, gave soluble fluoride complexes, or else yielded thorium fluoride as the insoluble phase. As the potassium fluoride concentration was increased, thorium fluoride was succeeded as solid phase first by KTh_2F_9 and then by α-K_2ThF_6. As found by Zachariasen, α-K_2ThF_6 was the major phase formed in all solutions rich in potassium fluoride, whether nitric acid was present or not.

The compound $KThF_5$ could not be isolated by observing conditions stated by Zachariasen, nor was it obtained at the expected composition between K_2ThF_6 and KTh_2F_9. It was obtained, however, in admixture with these compounds, in products precipitated in the absence of nitric acid by a large excess of potassium fluoride (Table 3). This suggests that it can be readily transformed into KTh_2F_9 by the action of nitric acid.

That KTh_2F_9 can also be changed in composition by the action of nitric acid is shown by the results in Table 2 for precipitations with potassium, thorium, and fluorine in molar ratios 1 : 2 : 9. The effect of nitric on the composition of the precipitate can be explained by the nature of the equilibrium between thorium and fluoride ions, this equilibrium, and hence the solubility product of the precipitates, depending on the hydrogen ion concentration.

Contrary to recent statements in the literature, all the precipitated phases were found to be hydrated, usually retaining 1 or 2 moles of water per mole of thorium fluoride when dried in air to constant weight, and less than 1·0 mole of water after drying for 15 hr. at 110°. Gelatinous thorium fluoride, however, retained 2·5—3·5 moles of water when air-dried and 1—2 moles when oven-dried under similar conditions. As *X*-ray powder photographs of precipitated thorium fluoride could not be obtained unless the product was sufficiently aged, it may be noted that detection of this phase in mixtures is not always possible.

Dehydration of thorium fluoride and of the binary fluorides without appreciable loss of fluorine may be completed at atmospheric pressure by heating them for approximately 3 hours at 300° (Table 4). At higher temperatures fluorine is lost, presumably as hydrofluoric acid, and increasing quantities of oxyfluoride and oxide are formed. Loss of fluorine appears to occur more readily from thorium fluoride than from the potassium thorium fluorides.

(iii) *Structure of the Potassium Thorium Fluorides.*—With the exception of the compounds α- and β-K_2ThF_6 (Zachariasen, *loc. cit.*; *Acta Cryst.*, 1949, **2**, 388), little detailed knowledge exists of the structure of the potassium thorium fluorides. There are, however, many points of similarity between the systems KF–ThF_4 and KF–UF_4 (Zachariasen, *loc. cit.*). Much simpler systems characterised by a few structures stable over a wide range of composition are formed if the central ion is much smaller than the potassium or thorium ions, *e.g.*, in the system KF–MgF_2 (Remy and Seemann, *Rec. Trav. chim.*, 1940, **59**, 516), or if the central ion is comparable in size to these ions, *e.g.*, in the system KF–LaF_3 (Zachariasen, *loc. cit.*). The exceptional complexity of the systems KF–ThF_4 and KF–UF_4 appears to be largely due to the values of the radius ratios K : Th and K : U, which fall between the ratios K : Mg and K : La.

There is no evidence that water in the precipitated binary fluorides plays an essential part in the structure of the compounds as the structures of the fused and of the precipitated fluorides are virtually identical. Water, however, may exert a stabilising influence on the structure of α-K_2ThF_6 since this phase if anhydrous should not be stable below 645°. Indeed, if water is completely removed from α-K_2ThF_6 by heating it to 300°, differential thermal analysis shows that the fluoride reverts *exothermically* to the β-form at approximately 400°. This product then undergoes the usual endothermic β- to α-transition at the equilibrium transition temperature of 645°. Many other binary potassium fluorides, *e.g.*, those of titanium, zirconium, and tin, resemble the potassium thorium fluorides in containing 1—2 moles of water which do not appear to form an essential portion of the crystal structure. Water in the thorium compounds, and possibly in analogous compounds, is presumed to occupy vacant sites in the crystal structures and may therefore be described as " lattice water."

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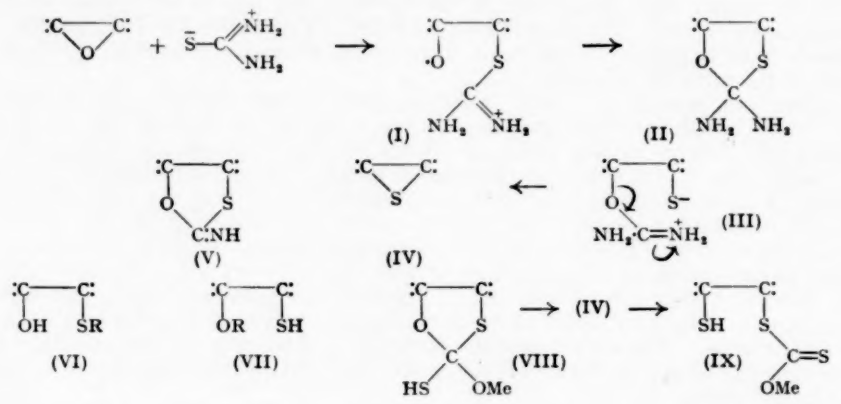
858. *The Conversion of Ethylene Oxides into Ethylene Sulphides.*

By C. C. Culvenor, W. Davies, and W. E. Savige.

The mechanism of the formation of ethylene sulphides by the interaction of ethylene oxides with certain actual or potential thiols, RSH, is discussed and shown to involve a transformation of the type $CH_2(OH)\cdot CH_2\cdot SR \longrightarrow CH_2(OR)\cdot CH_2\cdot SH$. The requirements of R for ethylene sulphide formation are defined and the wide scope of the reaction indicated. It is found that 2-(2 : 4-dinitrophenylthio)alkan-1-ols and other related nitro-compounds decompose in the same way in the presence of alkali to give ethylene sulphides which are largely polymerised, together with the corresponding nitrophenol. The reaction is also shown by 2-hydroxyethyl ethyl thiolcarbonate.

The study of the conversion of ethylene oxides into ethylene sulphides by means of alkali thiocyanates (van Tamelen, *J. Amer. Chem. Soc.*, 1951, **73**, 3444; see also Ettlinger, *ibid.*, 1950, **72**, 4792) prompts the recording of our own observations on the above conversion by a variety of reagents.

An examination of the preparation of ethylene sulphides from ethylene oxides and thiourea (Dachlauer and Jackel, D.R.-P. 636,708) led to the following reaction mechanisms being developed (Culvenor, Ph.D.Thesis, Melbourne, 1948, p. 20). The existence of thiourea in the zwitter-ion form (Sidgwick's "Organic Chemistry of Nitrogen," 1937, pp. 286, 291) accounts for its ready attack on the ethylene oxide ring by means of a nucleophilic displacement reaction. The initially formed 2-hydroxy-sulphide (I) is then considered to rearrange through the cyclic intermediate (II) into the 2-mercapto-ether (III), which finally decomposes into urea and the ethylene sulphide (IV).



The formation of (IV) is therefore due to two favourable factors, first, the ability of R in $CH_2(OH)\cdot CH_2\cdot SR$ to migrate to the oxygen atom to form $CH_2(OR)\cdot CH_2\cdot SH$, and secondly, the ready displacement of OR in this substance by the negatively charged sulphur atom. In general this is not the case, *e.g.*, if R = H or alkyl, compounds of this type are stable to ordinary alkaline conditions, but when $R = \cdot C(:NH)\cdot NH_2$, as in (III), there is a weakening of the C–O bond (as shown) by an electron shift towards the amidine group, and hence the displacement of OR by the sulphur atom is facilitated. Thus the decomposition into urea and an ethylene sulphide may be viewed as the simple electron redistribution shown in (III). Since this is quite different from the normal hydrolysis of an *O*-alkylurea, it is evident that a considerable part of the driving force is associated with the displacement of the urea grouping from carbon by the sulphur. There is another driving force in this formation of ethylene sulphides, *viz.*, the remarkable tendency to form a three-membered hetero-

cycle. This has not yet been satisfactorily explained, any more than in the case of the formation of ethylene oxides, where, contrary to ordinary conceptions of strain, an ethylene oxide can be formed as readily as a five-membered ring (Wilson, *J.*, 1945, 49). Finally, the fact that the ethylene sulphide produced is mainly the monomer is due to the alkali in the medium being so mild that the polymerisation to which ethylene sulphide is prone in alkali of somewhat higher concentration (Culvenor, Davies, and Heath, *J.*, 1949, 284; Coltof, U.S.P. 2,183,860, 1939; B.P. 508,932) occurs here only to a moderate extent.

This mechanism indicates that ethylene sulphides should result from the interaction of ethylene oxides with any thiol, RSH, and hence from the general initial product (VI), provided the nature of R be such that the proposed electron shifts can occur—first, to permit the transient formation of the oxathiole ring intermediate and so effect rearrangement to (VII), and secondly, to produce the necessary weakening of the C–O linkage. The main purpose of the present paper is to demonstrate not only the limitations but also the wide scope of this reaction. Ethylene sulphide formation has already been shown to occur when ethylene oxides condense with potassium thiocyanate, thioamides [R = CMe:NH, CPh:NH, and C(OEt):NH], or substituted thioureas [R = C(NHPh):NH and C:N·CO·CH_2·CO·NH] (Culvenor, Davies, and Heath, *loc. cit.*), and in each of these instances R fulfils the requirements for the above mechanism to be applied. Thus with potassium thiocyanate, the hypothetical oxathiole derivative (V), which rearranges and yields (IV) and potassium cyanate, is postulated. This is the mechanism suggested for this particular reaction by Ettlinger (*loc. cit.*) and more fully expounded by van Tamelen (*loc. cit.*).

The preparation of ethylene sulphide by the interaction of aqueous sodium sulphide with 2-chloroethyl thiocyanate (Delépine, *Bull. Soc. chim.*, 1920, **27**, 740) involves a similar process—the thiocyanate instead of the cyanate ion being produced. This, and Delépine's reaction (*loc. cit.*) of sodium sulphide with ethylene dithiocyanates, are instances of the displacement from carbon, by a negatively charged sulphur atom, of sulphur attached to an electrophile.

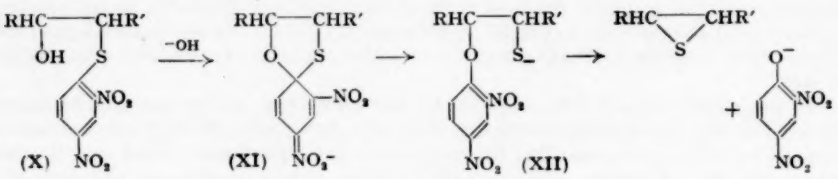
The mechanism of the interaction of ethylene oxide with potassium methyl xanthate [R = ·C(:S)OMe] to form ethylene trithiocarbonate (Culvenor, Davies, and Pausacker, *J.*, 1946, 1050) involves an intermediate (VIII) to explain the formation of (IV), which then reacts with more xanthate to give (IX), and thence the trithiocarbonate and potassium methoxide or hydroxide.

This trithiocarbonate formation can be faster than the polymerisation of an ethylene sulphide; for example, whilst early attempts to make styrene sulphide gave material of high molecular weight, styrene oxide with potassium methyl xanthate gave styrene trithiocarbonate in 77% yield (Culvenor, Davies, and Pausacker, *loc. cit.*; cf. Guss and Chamberlain, *J. Amer. Chem. Soc.*, 1952, **74**, 1342). It is considered then that the essential reaction pattern is the same, *viz.*, the transformation (VI) ⟶ (VII) ⟶ (IV), regardless of whether (IV) is isolated as the monomer, as a polymer, or as a trithiocarbonate as above—or even if isolated in the form of its decomposition products, as exemplified by the conversion of stilbene oxide by thiourea into stilbene and sulphur (together with urea) (cf. Culvenor *et al.*, *J.*, 1949, 2573).

The Smiles rearrangement of ether thiols into phenol sulphides in basic media (Warren and Smiles, *J.*, 1931, 914; Kon, *Ann. Reports*, 1933, **30**, 188; Watson, *ibid.*, 1939, **36**, 198) is essentially the reverse of the change (VI) ⟶ (VII). The proof (Coats and Gibson, *J.*, 1940, 442) of the reversibility of the Smiles rearrangement shows, however, that it is closely allied to the change (VI) ⟶ (VII) (which may itself prove to be reversible). Generally, attachment at a " positive " carbon of an aryl group is a condition of the Smiles rearrangement, and experimental evidence for the inherent analogy of the two processes is now found in the formation of ethylene sulphides from compounds of type (VI) where R is *o*-$C_6H_4(NO_2)$, 2 : 4-$C_6H_3(NO_2)_2$, or 2 : 4 : 6-$C_6H_2(NO_2)_3$. Simple ethylene oxides interact with 2 : 4-dinitrothiophenol to give crystalline 2-(2 : 4-dinitrophenylthio)alkan-1-ols (cf. Davies and Savige, *J.*, 1951, 774), which are also obtained from the interaction of the requisite thiol and 1-chloro-2 : 4-dinitrobenzene, in the presence of an exactly equivalent

amount of sodium hydroxide solution, or better by the use of such weak bases as sodium hydrogen carbonate, pyridine, or sodium acetate. (The analogous picryl derivatives are similarly obtained by use of picryl chloride.) Though the resulting sulphides are stable in acid or neutral media, they are converted by dilute alkali even in the cold into the di- or tri-nitrophenol and the corresponding ethylene sulphide. The reaction has been effected starting with ethylene, propylene, *iso*butylene, and *cyclo*hexene oxides, although the monomeric sulphides have as yet been detected mainly by means of their highly characteristic odours. The appropriate nitrophenol is readily isolated in high yield, and ethylene sulphide itself is obtained as the solid polymer. If 2-(2 : 4-dinitrophenylthio)*cyclo*hexan-1-ol (X; RR′ = •[CH_2]$_4$•) is warmed with alcoholic alkali in the presence of added carbon disulphide (to form potassium ethyl xanthate), *cyclo*hexene trithiocarbonate is obtained in good yield. This product demonstrates the formation of *cyclo*hexene sulphide in the reaction mixture since it is not readily formed from 2-mercapto*cyclo*hexanol under the same conditions. Potassium 2 : 4-dinitrothiophenoxide and stilbene oxide react to give 2 : 4-dinitrophenol and stilbene, and there is little doubt that the reaction proceeds analogously to that of stilbene oxide and thiourea.

The alkaline decomposition of 2-(2 : 4-dinitrophenylthio)alkan-1-ols (X) is considered to take the following path :

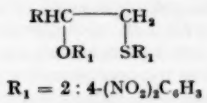


We have obtained definite evidence for the intermediate formation of the mercapto-ether (from ion XI) by carrying out the decomposition of (X; R = R′ = H) in the presence of 1-chloro-2 : 4-dinitrobenzene, the ether sulphide 1-(2 : 4-dinitrophenoxy)-2-(2 : 4-dinitrophenylthio)ethane [XIII; R = H] being isolated in 74% yield. Competition occurs between fixation of the intermediate (XII) as the diaryl derivative (as XIII) and the normal decomposition of (XII), since some ethylene sulphide and 2 : 4-dinitrophenol are also formed. Similarly, treatment of 1-(2 : 4-dinitrophenylthio)propan-2-ol (X; R = Me, R′ = H) with one mole each of 1-chloro-2 : 4-dinitrobenzene and alkali leads to a 50% yield of 2-(2 : 4-dinitrophenoxy)-1-(2 : 4-dinitrophenylthio)propane [XIII; R = Me], together with some of the usual products—propylene sulphide and dinitrophenol. It is clear that the diaryl (XIII) is formed from the ether thiol (as VII), and its isolation in considerable quantity shows that these thiol intermediates are sufficiently stable to persist in the reaction medium for a significant period of time. This conclusion should apply also to the general intermediate (VII) in other cases of ethylene sulphide formation, and it is probable that other thiols of this type can be isolated as derivatives in a similar way.

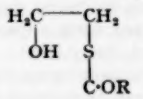
The reversed Smiles rearrangement, (X) ⟶ (XII), was tentatively studied by Kent and Smiles (*J.*, 1934, 422) with 2-*o*-nitrophenylthioethanol but they reported this compound to be stable to alkali. Hence they considered 2-hydroxy-sulphides to be the more stable isomers under alkaline conditions. We find that, although 2-*o*-nitrophenylthioethanol is very much more stable than the corresponding dinitro-compound, it does decompose to ethylene sulphide polymer and *o*-nitrophenol when refluxed with alcoholic alkali. The rearrangement cannot be detected with the compound (X; R = CH_2Cl, R′ = H) obtained from 2 : 4-dinitrothiophenol and epichlorohydrin, since it is known to be resistant to cold dilute alkali, and to produce 1-(2 : 4-dinitrophenylthio)-2 : 3-epoxypropane with concentrated alkali (Davies and Savige, *loc. cit.*). This is presumably due to the epoxide ring closure's being faster than the rearrangement.

Compounds of the type (VI; R = CO_2Et) also gave ethylene sulphide. Thus mercaptoethanol and ethyl chloroformate in pyridine gave the expected 2-hydroxyethyl thiolcarbonate (XIV; R = OEt), mixed with a smaller amount of the 2-mercaptoethyl

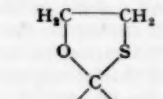
carbonate (XVI; R = OEt). These substances were not separated by distillation, but all fractions obtained produced ethylene sulphide when treated with alkali. An attempt to characterise the thiol (XVI; R = OEt) with chlorodinitrobenzene and alkali led to isolation of a small amount of the bis-2 : 4-dinitrophenyl compound (XIII; R = H). Evidently this was formed from the expected dinitrophenyl derivative of (XVI; R = OEt) by hydrolysis to give (X; R = R′ = H), and subsequent reaction of this substance as described above.



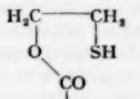
(XIII)



(XIV)



(XV)



(XVI)

Very recently, Harding, Miles, and Owen (*Chem. and Ind.*, 1951, **42**, 887) * have reported the isolation of monomeric ethylene sulphides from the decomposition of acetylated 2-hydroxy-thiols (VI; R = CO·CH_3) with weak alkali. They also regard the reaction as proceeding in the manner (XIV) ⟶ (XV) ⟶ (XVI; R = Me). Nylen and Olsen (*Chem. Abstr.*, 1942, **36**, 753) described the formation from ethylene oxide and thiolacetic acid of the thiolacetate (XIV; R = Me) and the isomerisation of the latter to (XVI; R = Me) by long heating with water. This with N-sodium hydroxide furnished a compound which the analysis and properties show to be polymeric ethylene sulphide. Sjöberg (*Ber.*, 1941, **74**, 64; 1942, **75**, 15) has also obtained compounds such as (XIV) by condensation of thiolacetic acid with epichlorohydrin, glycidol, and propylene oxide, severally, and although he did not study their behaviour towards alkali, he found that the acetyl group migrated spontaneously from sulphur to oxygen. He postulated for this change the " hypothetical intermediate " of type (XV).

Experimental

2-(2 : 4-Dinitrophenylthio)alkan-1-ols and Related Compounds.—Ethylene oxide was passed into a solution of 2 : 4-dinitrothiophenol in aqueous sodium hydrogen carbonate to give an immediate precipitate of 2-(2 : 4-dinitrophenylthio)ethan-1-ol (X; R = R′ = H), m. p. 100° (after recrystallisation from aqueous alcohol), identical with samples prepared from 1-chloro-2 : 4-dinitrobenzene and mercaptoethanol (Bennett and Whincop, *J.*, 1921, **119**, 1864), and from 2 : 4-dinitrothiophenol and ethylene chlorohydrin in aqueous sodium hydrogen carbonate.

2-(2 : 4-Dinitrophenylthio)*cyclo*hexan-1-ol (X; RR′ = ·$[CH_2]_4$·) (0·2 g.) was obtained by adding *cyclo*hexene oxide (0·1 g.) to a solution of 2 : 4-dinitrothiophenol (0·2 g.) in alcoholic sodium acetate, warming the mixture at 60° for 30 min., and then keeping it at room temperature for 16 hr. with exclusion of air. Crystallisation from aqueous alcohol gave small orange needles, m. p. 135°, undepressed on admixture with a specimen obtained from 2-mercapto*cyclo*hexanol and chlorodinitrobenzene (Culvenor, Davies, and Heath, *loc. cit.*). It may also be prepared by heating *cyclo*hexene oxide and dinitrothiophenol in alcohol for 12 hours at 55—60°. The similar derivatives from reaction of dinitrothiophenol with propylene and *iso*butylene oxides and epichlorohydrin were prepared according to Davies and Savige (*loc. cit.*).

Action of Alkali on 2-(2 : 4-Dinitrophenylthio)ethan-1-ol and Related Compounds.—On mixing at room temperature of alcoholic solutions of (X; R = R′ = H) (1·2 g.) and potassium hydroxide (0·28 g., 1 mol.), a bright red coloration was immediately produced, which faded to yellow within 10 seconds. There was a strong odour of ethylene sulphide, and potassium dinitrophenoxide separated. After a few minutes water was added, and the amorphous pale yellow precipitate (0·11 g.) was shown by analysis to be impure ethylene sulphide polymer. The filtrate after acidification yielded 2 : 4-dinitrophenol (0·82 g.), m. p. and mixed m. p. 111—112°. The first runnings of an aqueous-alcoholic distillate obtained by gently warming a suspension of (X) in 10% alcohol containing more than 1 mol. of sodium hydroxide were shown to contain ethylene sulphide by its odour, its instant reaction with the iodine–sodium azide reagent, and the typical separation of polymer noticeable 5 minutes after the addition of a trace of alkali. After 12

* This work is amplified by Miles and Owen, *J.*, 1952, 817, which arrived after the present paper was prepared for publication.

hours the polymer was washed with water and alcohol. Although the m. p. (165—175°) of the dry substance was high, the substance was practically pure polymer and had the characteristic property of electrifying strongly when rubbed with glass [Found; C, 40·1; H, 6·15. Calc. for $(C_3H_4S)_x$: C, 40·0; H, 6·7%].

A cold aqueous-alcoholic solution of 1-(2 : 4-dinitrophenylthio)propan-2-ol (Davies and Savige, *loc. cit.*, p. 321) and sodium hydroxide gave a red colour which faded to yellow in less than 1 minute. One portion of the mixture with dilute hydrochloric acid gave 2 : 4-dinitrophenol, another portion with concentrated hydrochloric acid gave this and the highly unpleasant odour of a 2-chloro-thiol, and a third portion on warming gave the not unpleasant odour of propylene sulphide. Results similar to the above were obtained with 1-(2 : 4-dinitrophenylthio)-2-methylpropan-2-ol (Davies and Savige, *loc. cit.*, p.778). Though with cold 40% aqueous sodium hydroxide, 1-chloro-3-(2 : 4-dinitrophenylthio)propan-2-ol gave the corresponding 2 : 3-epoxide (Davies and Savige, *loc. cit.*, p. 778), it was unchanged by cold 10% sodium hydroxide, but boiling with this alkali, or with aqueous potassium carbonate, gave a brown, amorphous precipitate. No 2 : 4-dinitrophenol was isolated, and the odour of chloropropylene sulphide was not detected.

Action of Alkali on 2-(2 : 4-*Dinitrophenylthio*)cyclo*hexan*-1-*ol*.—(i) Addition of an equivalent amount of 10% aqueous sodium hydroxide to an alcoholic solution of (X; RR′ = ·$[CH_2]_4$·) produced a bright red colour, fading to yellow within 5 min. The odour of *cyclo*hexene sulphide was recognised and crystals which soon separated were identified as sodium dinitrophenoxide since they were water-soluble, exploded before melting, and yielded 2 : 4-dinitrophenol on treatment with acid.

(ii) A mixture of (X; RR′ = ·$[CH_2]_4$·) (1·5 g.), carbon disulphide (0·4 ml.), and sodium hydroxide (0·4 g.) in alcohol (20 ml.) was heated for 5 min., kept for another 30 min., and then acidified with dilute sulphuric acid. The resulting oily yellow solid was washed with sodium carbonate solution and then crystallised from benzene to give *cyclo*hexene trithiocarbonate (0·52 g.), m. p. 164—165°, mixed m. p. 166—168°.

Preparation of 2-(2 : 4-*Dinitrophenoxy*)-1-(2 : 4-*dinitrophenylthio*)*propane* (XIII; R = Me).—(X; R = Me, R′ = H) (1·3 g.) and 1-chloro-2 : 4-dinitrobenzene (1·0 g., 1 mol.) were dissolved in alcohol (25 ml.) and treated with a solution of potassium hydroxide (0·28 g.) in alcohol (10 ml.). The reaction appeared to be similar to that performed in the absence of chlorodinitrobenzene. The colour of propylene sulphide was again clearly recognised. After 15 min., water was added, and the precipitate (1·9 g.) collected and crystallised from acetone to give 2-(2 : 4-*dinitrophenoxy*)-1-(2 : 4-*dinitrophenylthio*)*propane* (0·98 g.), yellow tabular prisms, m. p. 193—194° (Found: C, 42·7; H, 2·8; N, 13·2; S, 7·5. $C_{15}H_{12}O_9N_4S$ requires C, 42·5; H, 2·8; N, 13·2; S, 7·55%). Although sparingly soluble in most solvents, it dissolves to a considerable extent on refluxing in acetone for several hours. The reaction filtrate was concentrated to a small volume and acidified to give 2 : 4-dinitrophenol (90 mg.), m. p. 110—111°, mixed m. p. 111—112°.

1-(2 : 4-*Dinitrophenoxy*)-2-(2 : 4-*dinitrophenylthio*)*ethane* (XIII; R = H).—(X; R = R′ = H) (0·6 g.) and chlorodinitrobenzene (0·5 g., 1 mol.) were dissolved in alcohol (15 ml.) and treated with potassium hydroxide (0·15 g.) in alcohol (10 ml.). Water was added after 30 min. and the precipitate (0·77 g.) was collected and crystallised from acetone, giving 1-(2 : 4-*dinitrophenoxy*)-2-(2 : 4-*dinitrophenylthio*)*ethane* as pale yellow felted needles, m. p. 181—182°, sparingly soluble in alcohol, soluble in dioxan (Found: C, 41·3; H, 2·5; N, 13·2; S, 7·8. $C_{14}H_{10}O_9N_4S$ requires C, 41·0; H, 2·4; N, 13·7; S, 7·8%.)

2-(o-*Nitrophenylthio*)*ethan*-1-*ol*.—When (X; R = R′ = H) (0·2 g.), obtained from mercaptoethanol and *o*-bromonitrobenzene according to Bennett and Berry (*J.*, 1927, 1666), was refluxed for 15 minutes in alcohol (2 ml.) and water (0·25 ml.) containing sodium hydroxide (0·04 g.), it was nearly all recovered unchanged, although on acidification the odour of *o*-nitrophenol was apparent. However, after 3 hours' refluxing, a precipitate of ethylene sulphide polymer (0·06 g.) separated, and concentration and acidification of the filtrate furnished *o*-nitrophenol, m. p. and mixed m. p. 44°.

In this drastic experiment the formation of the ethylene sulphide polymer and not the fission of the sulphur–phenyl link is important. Thus it is found that in a comparable experiment the refluxing for 1 hour of 2 : 4-dinitrothioanisole with alcoholic potassium hydroxide produced 2 : 4-dinitrophenol and dimethyl disulphide, as well as an intense darkening of the reaction mixture.

2-*Picrylthioethanol and Related Compounds*.—2-*Picrylthioethanol*, m. p. 72°, small yellow needles from benzene–ligroin (Found: N, 14·9. $C_8H_7O_7N_3S$ requires N, 14·55%), was obtained

on gradually adding a solution of sodium acetate (1 g.) in alcohol (20 ml.) to a mixture of picryl chloride (2·5 g.) and 2-mercaptoethanol (0·8 g.) in alcohol (20 ml.), then warming it on the water-bath for 10 minutes, and finally diluting it with water. Each addition of sodium acetate produced a red colour, which soon faded. The same product was obtained when sodium hydroxide (0·4 g.) in alcohol was used in place of sodium acetate, the mixture being well shaken after each addition.

With excess of alcoholic alkali, 2-picrylthioethanol gave a deep crimson colour which did not completely fade during 10 minutes, but rapidly changed to pale yellow on slight warming. A yellowish, polymeric precipitate was obtained, and the odour of ethylene sulphide was detected. Acidification of the mixture with concentrated hydrochloric acid gave rise to the unpleasant odour of a chloro-thiol, together with precipitation of picric acid (identified by mixed m. p.).

2-Picrylthioethanol in glacial acetic acid was warmed at 100° for 6 hours with a slight excess of 30% hydrogen peroxide; the mixture was then diluted with water, and extraction with chloroform gave a large proportion of picric acid. Treatment of 2-picrylthioethanol in acetone with 30% hydrogen peroxide for 2 weeks at 30° brought about the separation of a large quantity of acetone peroxide, prisms, m. p. *ca.* 95°. No other product was isolated. 1-Picrylthiopropan-2-ol and 2-chloro-1-picrylthiopropane (Davies and Savige, *J.*, 1950, 321, 322) gave similar results to 2-picrylthioethanol, on treatment with hydrogen peroxide.

Ethyl picryl sulphide, m. p. 44—45°, long yellow needles from methanol (Found: N, 15·2. $C_8H_7O_6N_3S$ requires N, 15·35%), was obtained when a solution of pyridine (0·4 g.) in alcohol was added to a mixture of ethanethiol (0·3 g.) and picryl chloride (1·25 g.) in alcohol (a deep red colour was first obtained; this soon disappeared with formation of a black, granular precipitate), then the mixture was warmed on the water-bath for 15 minutes (a clear, yellow solution being obtained), allowed to cool, and diluted with a small amount of water. The sulphide is unchanged on warming with 10% aqueous alcoholic sodium hydroxide. It is converted by 30% hydrogen peroxide in glacial acetic acid (1 hour at 100°) into *ethyl picryl sulphoxide*, m. p. *ca.* 175° (violent detonation), yellow prisms from acetic acid (Found: N, 14·4. $C_8H_7O_7N_3S$ requires N, 14·55%). *Ethyl picryl sulphone*, m. p. *ca.* 210° (slight decomp.), pale yellow plates from acetone–ligroin, was obtained on warming ethyl picryl sulphide for 5 hours at 100° with 30% hydrogen peroxide in glacial acetic acid (Found: N, 13·8. $C_8H_7O_8N_3S$ requires N, 13·8%).

Trityl Thioethers.—*2-(Triphenylmethylthio)ethanol*, m. p. 114—115°, plate-like needles from ligroin (Found: C, 78·75; H, 6·6; S, 10·65. $C_{21}H_{20}OS$ requires C, 78·75; H, 6·25; S, 10·0%), was obtained on warming a mixture of triphenylmethyl chloride (2·4 g.) and mercaptoethanol (0·7 g.) in ligroin on the water-bath for 1 minute (hydrogen chloride being evolved), and crystallising the crude product from aqueous alcohol. It was recovered unchanged after refluxing for 4 hours with alcoholic potassium hydroxide. This stability to alkali contrasts with its conversion into triphenylmethanol in 15 minutes on the water-bath by hydrochloric acid in aqueous dioxan. It also gave triphenylmethanol after long storage with dilute sulphuric acid or by treatment with phosphorus pentachloride in chloroform or by thionyl chloride and pouring the product into water. (The above products were identified by m. p. and mixed m. p. determinations.) Here the side chain in 2-(triphenylmethylthio)ethanol has evidently suffered fission, the triphenylmethyl chloride formed being hydrolysed to the carbinol by the water. This is indicated by the stability of 2 : 3-dichloropropyl triphenylmethyl sulphide (Davies and Savige, *loc. cit.*, p. 777) to glacial or aqueous acetic acid, and its ready conversion into triphenylcarbinol by chloroformic phosphorus pentachloride followed by aqueous treatment. The contrast between trityl and 2 : 4-dinitrophenyl thioethers is shown by the ready interaction of chloroformic phosphorus pentachloride and 1-(2 : 4-dinitrophenylthio)propan-2-ol to yield 2-chloropropyl 2 : 4-dinitrophenyl sulphide (VI) (cf. Davies and Savige, *loc. cit.*, p. 779).

Reaction of 2-Mercaptoethanol with Ethyl Chloroformate.—Ethyl chloroformate (9·8 ml., 10·85 g.) in dry ether (15 ml.) at 0° was added in portions, with frequent shaking, to a mixture of mercaptoethanol (7·8 g.) and pyridine (9 g.) in dry ether (15 ml.), contained in an ice-bath. A yellow colour was observed after each addition of ester, but this soon faded. The mixture was kept at 10°, with occasional shaking, for ½ hour, and plates of (presumably) pyridine hydrochloride then separated. The mixture was poured into water (50 ml.), and the ethereal layer separated, washed with water, dried (Na_2SO_4), and distilled. Constant-boiling fractions could not be obtained. In the initial distillation, three fractions were collected separately: (1) b. p. 48—50°/0·7 mm., n_D^{16} 1·488 (1 ml.), slightly soluble in cold water; (2) intermediate fraction, n_D^{16} 1·4654 (0·5 ml.); (3) b. p. 85—110°/0·4 mm., n_D^{16} 1·467 (10 ml.), soluble in warm water, but reprecipitated on cooling. The amount of higher-boiling material was negligible. All three fractions were mobile liquids, and each gave a mauve colour with aqueous sodium nitroprusside,

and possessed a mercaptan-like odour. Each of the fractions, when warmed with 10% aqueous sodium hydroxide, gave amorphous polymeric material, and evolved ethylene sulphide. Fraction (1) may have contained some mercaptoethanol: that used had n_D^{16} 1·4985, b. p. 52°/12 mm.

Fraction (3) was redistilled with the aid of an efficient fractionating column, but again a constant-boiling fraction could not be obtained. The distillate was divided arbitrarily into three equal fractions: (3*a*) b. p. 133—140°/20 mm.; (3*b*) b. p. 140—158°/20 mm., n_D^{15} 1·472 (Found: C, 40·15; H, 6·55. Calc. for $C_6H_{10}O_3S$: C, 40·0; H, 6·65%); (3*c*) b. p. 158—168°/20 mm., n_D^{15} 1·465. These three fractions are each considered to be a mixture, consisting mainly of ethyl *S*-2-hydroxyethyl thiolcarbonate (XIV; R = OEt), with a smaller amount of ethyl 2-mercaptoethyl carbonate (XVI; R = OEt). Each had properties similar to those described above for fraction (3), except that fraction (3*a*) partly polymerised to a white solid when kept in a sealed tube for 1 month (possibly caused by the alkali in the glass).

Reaction of the Condensation Product with p-*Nitrophenyl* iso*Cyanate.*—Fractions (3), (3*a*), (3*b*), and (3*c*) all gave the following reaction; it (0·5 g.) was warmed on the water-bath for 1 hour with a filtered solution of *p*-nitrophenyl *iso*cyanate (1·5 g.) in dry benzene (15 ml.), with exclusion of moisture. The cooled mixture was quickly filtered into a dry flask, and ligroin (15 ml.) added. When cooled to 0°, and rubbed with a glass rod, the precipitated oil solidified, giving a crude, pale yellow product, m. p. 95—98° (0·5 g.). Recrystallisation of this from benzene–ligroin gave a compound, considered to be 2-*carbethoxythioethyl* p-*nitrophenylcarbamate*, *p*-$NO_2{\cdot}C_6H_4{\cdot}NH{\cdot}CO_2{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CO_2Et$, m. p. 100·5°, large, pale ivory needles (Found: C, 46·1; H, 4·4; S, 10·05, 10·35. $C_{12}H_{14}O_6N_2S$ requires C, 45·8; H, 4·45; S, 10·2%); more was obtained on concentration of the original filtrate, but attempts to isolate a second product were unsuccessful.

Reaction of Condensation Product with 1-*Chloro*-2 : 4-*dinitrobenzene.*—Each of fractions (1), (2), (3), (3*a*), and (3*c*) gave the following reaction: The fraction (0·15 g.), 1-chloro-2 : 4-dinitrobenzene (0·2 g.), and sodium hydroxide (0·04 g.) in alcohol (10 ml.) were kept for 5 minutes. The precipitate was washed with alcohol, then with water, and finally recrystallised from glacial acetic acid and then from ethyl acetate, giving 1-(2 : 4-dinitrophenoxy)-2-(2 : 4-dinitrophenylthio)ethane, (XIII; R = H), m. p. and mixed m. p. 181—182°, fine, pale yellow needles (0·18 g.) (Found: C, 41·1; H, 2·6; S, 7·7; N, 13·1%). It is sparingly soluble in hot alcohol or in cold benzene, but soluble in dioxan. Addition of water to the original filtrate gave an oil, which appeared to be a mixture of unchanged reactants. However, no additional product was obtained on keeping this mixture.

Action of Potassium 2 : 4-*Dinitrothiophenoxide on Stilbene Oxide.*—Stilbene oxide (0·6 g.) was added to a solution of dinitrothiophenol (0·61 g.) and potassium hydroxide (0·17 g.) in alcohol (5 ml.) and kept at 32° for 2 days. The mixture was diluted with water, and the resulting oily precipitate crystallised from a little alcohol and sublimed, to furnish stilbene as colourless prisms, m. p. and mixed m. p. 124°. The aqueous filtrate was evaporated to a small volume, acidified, and extracted with ether. This extract yielded 2 : 4-dinitrophenol, m. p. 108—110°, mixed m. p. 111°.

The micro-analyses were made in Dr. Zimmermann's laboratory in the Commonwealth Scientific and Industrial Research Organization, Melbourne. One of us (W. E. Savige) acknowledges financial assistance from the Commonwealth Reconstruction Training Scheme.

UNIVERSITY OF MELBOURNE. [*Received, June 13th*, 1952.]

859. *Studies on Unimolecular Chlorohydrocarbon Decompositions. Part III.**

By K. E. Howlett.

A marked relationship between the Arrhenius parameters, A and E, is observed for the rate-constant equations for unimolecular pyrolysis of the monochloroalkanes. This is examined quantitatively from the activated-complex and the energy-accumulation theories of reaction. The thermal decomposition of *iso*butyl chloride is shown to be a homogeneous unimolecular dehydrochlorination for which $k = 10^{14\cdot02}\,e^{-56850/RT}$. The correlations predicted from the alternative explanations of unimolecular processes are tested by application to this reaction and to the decompositions of *tert.*-butyl and *n*-propyl chlorides. The better agreement is found with the idea that the slow stage of a unimolecular reaction consists of the concentration of energy transforming activated molecules into reacting molecules. The anomalous values of A and E for pyrolysis of ethylidene dichloride compared with those of the monochloroalkane decompositions are discussed.

Barton and Head (*Trans. Faraday Soc.*, 1950, **46**, 114) and Barton, Head, and Williams (*J.*, 1951, 2039) have drawn attention to the marked correlation which exists between the parameters, A and E, of the Arrhenius rate-constant equation for the homogeneous unimolecular decompositions of the simple monochloroalkanes. A fair range of the variables shows a direct, approximately linear relation between $\log_{10} A$ and E. Somewhat analogous correlations in other series of reactions have been observed, and such behaviour has been critically discussed before (see, *e.g.*, Evans and Polanyi, *Trans. Faraday Soc.*, 1936, **32**, 1333; Fairclough and Hinshelwood, *J.*, 1937, 538, 1573, and references there cited; Gregg and Mayo, *Discuss. Faraday Soc.*, 1947, **2**, 328; Cremer, *Experientia*, 1948, **4**, 349; Bamford and Dewar, *Nature*, 1949, **163**, 256; Christiansen, *Acta Chem. Scand.*, 1949, **3**, 61; Bernstein, *J. Chem. Physics*, 1952, **20**, 524) but no example investigated is a homogeneous gaseous reaction. Indeed, Szwarc (*Chem. Reviews*, 1950, **47**, 108) has denied the significance of correlation in this instance.

In the series under discussion, very poor agreement is found between the experimental activation energies and those calculated by means of the empirical equation proposed by Fugassi and Warrick (*J. Phys. Chem.*, 1942, **46**, 630). These authors have sought to describe the activation energy for a reaction where two bonds are broken, in terms of the vibration frequency and bond energy of the weakest bond ruptured. Table 1 gives the values of $\bar{\nu}$

Table 1.

Substance	D(C–Cl) (kcal./g.-mol.)	$\bar{\nu}$, cm.$^{-1}$	E (calc.) (kcal./g.-mol.)	E (obs.)
EtCl	80·4	650	52·4	60·8
Pr^{i}Cl	77·9	612	49·7	50·5
Bu^{t}Cl	75·3	570	46·7	41·4

and D(C–Cl) (including the zero-point energy) employed in these calculations, and shows the inadequacy of this treatment as applied to typical eliminations of hydrogen chloride.

The purpose of this paper is to examine the observations amongst dehydrochlorination reactions from the point of view of the mechanism of unimolecular reactions. The reaction model must therefore be defined. It is useful to regard unimolecular processes as consisting of the three steps, collisional activation, energy concentration in a particular location, and passage over the energy barrier (mechanical dissociation or rearrangement) to products (cf. references in Part II *). Eley (*Trans. Faraday Soc.*, 1943, **39**, 168) has suggested that a distinction between the possible slow stages of this scheme, steps 2 or 3, might be obtained experimentally from the sign of dE/dT when $\log_{10} A > 13$, although admittedly the difficulty of assessing an accurate value for E over a limited temperature range is great. This

* Part II, 1952, 3695.

test can only be applied to the four unimolecular dehydrochlorinations of ethyl, *n*-butyl and *iso*butyl chlorides (see Experimental section) and of 1 : 2-dichloropropane, for which the calculated values of the entropy of activation are positive. The last example is unsuitable for discriminative work owing to the small temperature range over which the decomposition has been studied. In the other three cases the Arrhenius activation energies have been recalculated over the upper and lower halves of the temperature ranges investigated. The results are inconclusive, dE/dT being respectively positive, 0, and negative, and giving a mean figure of +10 cal./deg. g.-mol.

The decompositions of ethyl, *n*- and *iso*-propyl, and *n*- and *tert.*-butyl chlorides were therefore first considered from the activated-complex theory, their rate equations being rewritten in the form $k_r = e(kT/h)e^{-E_{exp.}/RT}\, e^{\Delta S^{\ddagger}/R}$ (Glasstone, Laidler, and Eyring, "Theory of Rate Processes," McGraw-Hill, 1941). The transmission coefficient has been neglected, but would make no difference to the conclusions, provided its variation is not large. Quantum-mechanical calculations indicate that, in the absence of other interactions, eliminations of this type will proceed through a four-centre planar transition state (cf. *e.g.*, Penney, "Quantum Theory of Valency," Methuen, 1935, p. 82; Barton, *J.*, 1949, 2174). Thus, in the activated state, the carbon atoms which will become doubly bound and their associated groups resemble an eclipsed ethane structure, so that the two permanently bound pairs of substituents are also at the position of closest approach. The rotation of alkyl-substituted methyl groups about C–C bonds is more energetically hindered than that of unsubstituted groups (Pitzer, *J. Amer. Chem. Soc.*, 1948, **70**, 2140; Howlett, *J.*, 1951, 1409). These restrictions might therefore increase the activation energy or lower the non-exponential term by affecting the entropy of activation. Comparison with the known rate equations shows that no correlation can be traced with the former possibility. Further, a simple statistical effect might be operative, somewhat analogous to that cited by Szwarc concerning the pyrolyses of *p*-xylene and toluene (*J. Chem. Physics.*, 1948, **16**, 128). The chlorine atom in the monochloroalkanes can eliminate with a variable number of hydrogen atoms, *e.g.*, 2 in *n*- and 9 in *tert.*-butyl chloride. If this is significant, then this statistical factor should be included in the rate equation. $\Delta S^{\ddagger}$ has been calculated for the operation of the first, and of both these effects in monochloroalkane pyrolyses and is compared with the transition-state non-bonded interactions in Table 2. Correlation may

TABLE 2.

Substance	$\Delta S^{\ddagger}$	Modified $\Delta S^{\ddagger}$	Non-bonded interactions
EtCl	4·5	3·1	2 H···H
Pr^{n}Cl	−0·73	−1·7	1 H···H
Pr^{i}Cl	−0·79	−3·5	+ 1 H···Me (or Et)
Bu^{n}Cl	1·8	0·85	
Bu^{t}Cl	−5·1	−9·3	2 H···Me

exist between both $\Delta S^{\ddagger}$ cols. and col. 4.

Turning to the alternative explanation of unimolecular reactions—that step 2 is rate determining—an interesting parallel may be observed by applying the mathematical theory of Rice and Ramsperger (see Part II). For each of the decompositions treated in Part II, the number of square terms contributing towards the activation energy has been determined. Thus the fractional contribution towards the rate constant for any specified molecular energy in excess of E may be calculated. The necessary integrations have been carried out for 1 : 1-dichloroethane at 412°, *iso*propyl chloride at 406·6°, and ethyl chloride at 456°. Comparison of the first curve with that given previously for the same compound at 449° shows that the $(\varepsilon - \varepsilon_0)$ value at maximum k_ε lies at an approximately constant value (8·5 kcal./g.-mol. at 412°, 9 at 449°). The results for the various reactions may therefore be compared, despite the fact that they refer to different temperatures and rates.

For any one decomposition it is found that the contribution of the partial rate constant k_ε increases with $(\varepsilon - \varepsilon_0)$ up to moderate energy excesses, because the decreased time t (Fairclough and Hinshelwood, *loc. cit.*) between activation and spontaneous reaction outweighs the decreased probability of such a high energy state. For large energy excesses, of course, when t is very small and capable of little further variation, the extreme improb-

ability of the state ensures that the contribution to reaction again approaches zero. Thus when comparing different decompositions, it is reasonable to suppose that, up to a limit, the non-exponential terms will vary directly with the values of $(\varepsilon - \varepsilon_0)$ at maximum k_ε. The three reactions already studied show just this correlation (Table 3).

TABLE 3.

	$Me{\cdot}CHCl_2$	Pr^iCl	EtCl
$\log_{10} A$	11·65	13·5	14·7
$(\varepsilon - \varepsilon_0)$ (kcal./g.-mol.) at max. k_ε	9	15	18·5

In order to discriminate between these alternative explanations, the decomposition of *iso*butyl chloride, and low-pressure pyrolyses of *tert.*-butyl chloride and *n*-propyl chloride, have been investigated.

EXPERIMENTAL

Apparatus and Materials.—The apparatus used has been described in Part II (*loc. cit.*). The three chlorides were prepared by standard methods from the corresponding alcohols and purified by treatment with sulphuric acid, fractional crystallisation, and distillation (cf. Barton, Head, and Williams, *loc. cit.*). The following physical constants were measured: *iso*butyl chloride, b. p. 68·5° (corr.), n_D^{20} 1·3982; *tert.*-butyl chloride, b. p. 50·7° (corr.), n_D^{20} 1·3844; *n*-propyl chloride, b. p. 46·5° (corr.), n_D^{25} 1·3851.

RESULTS

iso*Butyl Chloride.*—It is first necessary to establish that pyrolysis of *iso*butyl chloride leads to dehydrochlorination, although this result is expected (Howlett, Thesis, London, 1948). The decomposition has been studied over the temperature range 361·5° to 475° and a number of long-term experiments, of duration > 20 times that required for half decomposition, have shown that, at various temperatures, the final pressure is close to twice that initially admitted (see Table 4). At the end of each of these runs, the pressure in the system fell to zero on connecting

TABLE 4.

Temp.	p_0, mm.	p_t/p_0	Temp.	p_0, mm.	p_t/p_0
417°	23·7	2·01	450°	3·07	2·00
429 *	4·77	1·98	450	5·55	2·03
431	4·96	2·08	452 *	30·4	2·06
438 *	63·2	1·97	463	3·45	2·00
444 *	20·3	2·00	474	2·77	2·03

* Packed reactor.

the reactor to a small, evacuated liquid-air trap. Titration of the condensate with standard alkali indicated 85—100% of the theoretical quantity of hydrogen chloride. Better quantitative agreement cannot be expected in this case (cf. Mayo and Katz, *J. Amer. Chem. Soc.*, 1947, **69**, 1339; Howlett, *J.*, 1951, 1409), and the absence of hydrogen in the products shows that only dehydrochlorination occurs.

Fig. 1 shows that at various temperatures, first-order kinetics are followed to a considerable percentage of reaction, and Table 5 shows that the rate constant at 450° is invariant with initial

TABLE 5.

p_0, mm.	10^5k, sec.$^{-1}$	p_0, mm.	10^5k, sec.$^{-1}$	p_0, mm.	$p_{C_3H_6}$, mm.	10^5k, sec.$^{-1}$
3·07	70	9·33	70	9·60	1·75	73
3·75	65	21·0	70	9·00	3·45	70
4·91	69	43·9	73	9·72	5·6	70
9·20	74	—	—	9·74	8·2	69

pressure above $p_0 = 3$ mm., and also unchanged by the addition of propene. Propene is well known as a strong inhibitor of radical-chain dehydrochlorinations.

The homogeneity of the reaction is demonstrated by the negligible increase in the rate constant, obtained by carrying out the decomposition in a reactor packed to a 10-fold increase in surface : volume ratio over that in the unpacked reaction vessel. These results are illustrated, together with the results obtained in an " empty " reactor in the Arrhenius plot, Fig. 2. The pyrolysis

of *iso*butyl chloride is therefore a clean homogeneous unimolecular dehydrochlorination. Table 6 lists the observed rate constants for decompositions in both empty and packed reactors. From the results given in Fig. 2 it may be calculated by the method of least squares, giving equal weight to each experiment, that $k = 10^{14\cdot02}\ e^{-56850/RT}$ for the pyrolysis of *iso*butyl chloride in an unpacked reactor, the walls of which are covered with a carbonaceous film. For decom-

FIG. 1.

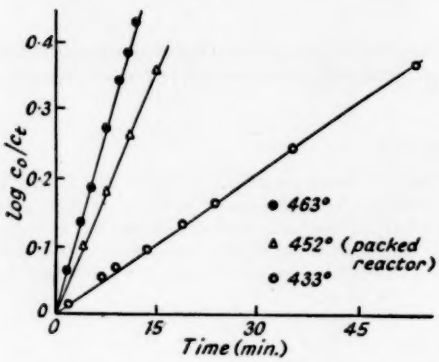


FIG. 2.

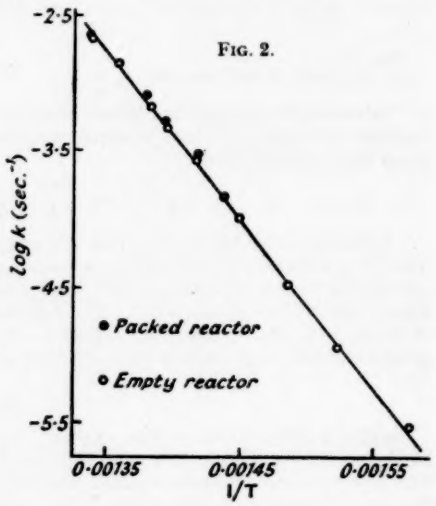
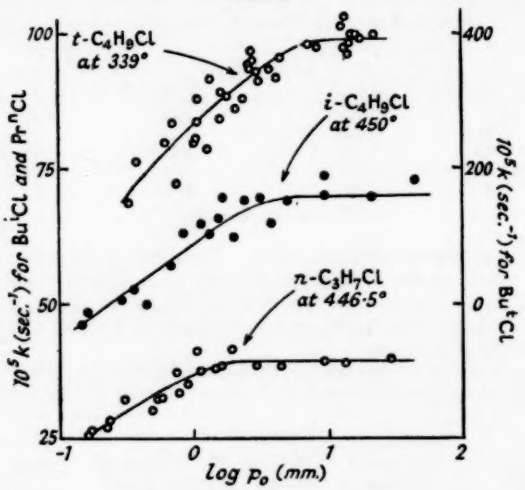


FIG. 3.



positions of initial pressure <3 mm. this equation is inapplicable because in this region the rate constant is a function of the pressure (see Fig. 3).

tert.-*Butyl Chloride and* n-*Propyl Chloride.*—Barton and Onyon (*Trans. Faraday Soc.*, **1949, 45,** 725) and Barton, Head, and Williams (*loc. cit.*) have given the rate equations $k = 10^{13\cdot4}\ e^{-41400/RT}$ and $10^{13\cdot45}\ e^{-55000/RT}$ for *tert.*-butyl and *n*-propyl chloride respectively. These rate constants refer to decomposition from initial pressure >50 mm. In the present study, the decomposition of *tert.*-butyl chloride has been examined at 339° and that of *n*-propyl chloride at 446·5°, in an attempt to find critical pressure regions in the k–p_0 graphs. In each case good agreement has been obtained with the previous work at high pressures (the velocity constants

TABLE 6.

Temp.	No. of runs	10^5k, sec.$^{-1}$	Temp.	No. of runs	10^5k, sec.$^{-1}$
Unpacked reactor.					
361·5°	2	0·30	444°	3	47·4
384	2	1·17	450	15	69·7
400	5	3·42	463	8	145
417	6	10·3	474	7	214
433	7	26·8	475	3	230
Packed reactor.					
422·5	3	15·0	444·5	4	53·6
432	4	30·5	452	5	82·8

calculated from the rate equations are respectively 0·00417 and 0·00055 sec.$^{-1}$). The results are shown in Fig. 3, which also depicts the results obtained with *iso*butyl chloride at 450°. The transitional regions found are *ca.* 6 mm. (Bu^{t}Cl), 1—1·5 mm. (Pr^{n}Cl), and 3 mm. (Bu^{i}Cl).

DISCUSSION

The values of $\log_{10} A$ and E for decomposition of *iso*butyl chloride lie close to the straight line correlating these quantities given by Barton, Head, and Williams (*loc. cit.*) for other chlorohydrocarbon pyrolyses. *iso*Butyl chloride cannot, however, be fitted to the correlation of Table 2. The chlorine atom in this compound can be eliminated with only the tertiary hydrogen atom, and the activated complex would have 2 H···Me non-bonded interactions. Both entries for $\Delta S^{\ddagger}$ in Table 2 for this compound are +1·65 E.U. in contrast to the values of *ca.* −5 or −9 expected if *iso*butyl chloride conformed to the suggested explanation of $\log_{10} A$ in terms of entropy of activation effects due to non-bonded interactions, and to the number of β-hydrogen atoms.

Better agreement is found with the second correlation. From the critical-pressure regions reported above, the numbers of classical oscillators contributing towards the activation energies are 10 (Bu^{t}Cl), 14½ (Pr^{n}Cl) and 14 (Bu^{i}Cl). By assuming in each case that the transformation probability of an activated molecule is a function of its energy content (cf. Part II), the appropriate integrations of Rice and Ramsperger's equation have been performed, and $(\epsilon - \epsilon_0)_{\text{max. } k_\epsilon}$ values of 11·5, 19·5, and 19·5 kcal./g.-mol. respectively found. Thus all six unimolecular dehydrochlorinations examined from this point of view show a reasonably systematic variation in $(\epsilon - \epsilon_0)_{\text{max. } k_\epsilon}$ with $\log_{10} A$, whilst 1 : 1-dichloroethane is inconsistent with the others when $\log_{10} A$ is plotted against E. This consistency of one correlation coupled with an anomaly in the other can be appreciated if a reaction of high activation energy tends to accumulate this energy from a large number of square terms, and *vice versa*. The participation of a large number of square terms shifts the maximum in the k_ϵ–$(\epsilon - \epsilon_0)$ curve to higher energy values, so that while the chlorohydrocarbon is of constant type, *i.e.*, one C–Cl bond in an otherwise paraffinic molecule, correlation of $\log_{10} A$ with $(\epsilon - \epsilon_0)_{\text{max. } k_\epsilon}$ implies correlation with E. When, however, the vibrational modes immediately adjacent to the reaction centre arise partly from an additional C–Cl bond, the anomalous behaviour is not surprising, for it has frequently been suggested (Rice, *Z. physikal. Chem.*, 1930, *B*, **7**, 226; Glasstone, Laidler, and Eyring, *op. cit.*, p. 287; Barrer, *Trans. Faraday Soc.*, 1948, **44**, 399) that the efficiency of energy transfer in a " vibrational collision " will vary with the nature of the two oscillators concerned. 1 : 1-Dichloroethane, with a larger number of low frequency vibrators near the reaction centre than (say) ethyl chloride, may thus be expected to show a different looseness of coupling between those oscillators which are the chief contributors towards the activation energy. If this is so, then the effective values of n and t (which determine $\log_{10} A$) at constant E, will be different for the decompositions of compounds of type >CH·CCl$_2$– and for those of the series >CH·CCl–.

My sincere thanks are offered to Professor E. E. Turner for his continuous interest and encouragement, and to Mr. R. J. Williams for helpful discussion.

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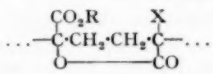
860. *The Pyrolysis of Poly-(sec.-butyl α-Chloroacrylate).*

By J. W. C. Crawford and D. Plant.

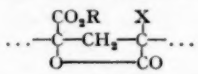
When poly-[(+)-*sec.*-butyl α-chloroacrylate] is pyrolysed, *sec.*-butyl chloride is formed as the result of a lactonization reaction. The configuration of the chloride is inverted, with about 40% racemization. Mechanisms for the lactonization reaction have been considered, and it is concluded that a "unimolecular" process involving the formation of butyl ions occurs at least to the extent of the racemization of the butyl chloride.

(+)-*sec.*-Butyl γ-chlorobutyrate, used as a model for the reactive units of the chloroacrylate polymer, forms, with inversion, *sec.*-butyl chloride of rotatory power similar to that obtained from the chloroacrylate polymer, but only when heated in presence of zinc chloride or similar catalyst.

During an investigation of the polymers of methyl α-chloro- and α-bromo-acrylates, Marvel and Cowan (*J. Amer. Chem. Soc.*, 1939, **61**, 3156) observed that, when pyrolysed, the bromoacrylate polymer evolved methyl bromide as well as hydrogen bromide. Polymerization of the methyl esters, or of other esters (*ibid.*, 1940, **62**, 3495), led on occasion to products which were low in halogen; they suggested that this might also be due to loss of alkyl halide. Loss of halide would result in formation in the polymers of lactone structures (I) or (II), according as the polymer had a head-to-head or head-to-tail structure. The head-to-head structure yielding the six-membered lactone ring (I) was preferred by the above authors on grounds of chemical behaviour of the polymers. The head-to-tail structure seems to be that more generally met with in ethenoid polymers.



(I)



(II)

Poly-[(+)-*sec.*-butyl α-chloroacrylate], derived from (+)-*sec.*-butanol, has been pyrolysed. Heated *in vacuo* at 190°, the polymer decomposed, yielding as volatile products butene, hydrogen chloride, *sec.*-butyl chloride, and probably some monomer formed by depolymerization. The butyl chloride was lævorotatory. Rotatory powers of the materials involved in the series of reactions are given below:

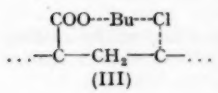
	$[\alpha]_D$	Temp.
(+)-*sec.*-Butanol	+15·1°	20°
(+)-*sec.*-Butyl α-chloroacrylate	+34·2	22
Poly-[(+)-*sec.*-butyl α-chloroacrylate] (solid)	+ 8·0	21·5
(−)-*sec.*-Butyl chloride	−22·2	21

Since *sec.*-butyl chloride of the same configuration as (+)-*sec.*-butanol is dextrorotatory (Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1268), it follows that in the series of reactions leading from butanol to butyl chloride, inversion occurred of the configuration of the butyl radical. The monomeric ester was prepared by esterification of (+)-*sec.*-butanol with α-chloroacrylic acid; the configuration of the butyl radical would be preserved in this reaction, apart from the possibility of very slight racemization. Polymerization of the monomeric butyl α-chloroacrylate would not affect the configuration of the butyl radical. The inversion must therefore have occurred during the pyrolysis, in the formation of butyl chloride by the lactonization reaction.

The possibility has been considered that butyl chloride might alternatively have been formed by reaction of the carbobutoxy-groups in the polymer with hydrogen chloride. The latter is formed in the pyrolysis of poly(methyl α-chloroacrylate), and can therefore arise by dehydrochlorination of the main polymer chain, with formation of ethylenic unsaturation in this. In the case of the pyrolysis of poly-(*sec.*-butyl α-chloroacrylate), hydrogen chloride could additionally arise from lactonization of the chloroacrylic acid units left in the polymer when butylene was evolved. Experiment indicated that butyl chloride

was unlikely to be formed in this way; *sec.*-butyl hexanoate, α-chloropropionate, and γ-chlorobutyrate, esters which might in some degree simulate the reactive units in the butyl chloroacrylate polymer, gave no butyl chloride (or butene) when heated with hydrogen chloride.

If the formation of butyl chloride in the pyrolysis of poly-(*sec.*-butyl α-chloroacrylate) proceeded solely by a "bimolecular" mechanism through the transition state (III) the butyl radical would undergo complete inversion of configuration, to yield fully active butyl chloride. One might suppose, as an alternative, that the butyl chloride could arise by formation of butyl ion from the carbobutoxy-group, followed by reaction of the ion with chlorine. The butyl chloride produced in this "unimolecular" reaction would be expected to be racemized, or partially racemized with inversion (owing to screening of the butyl by the carboxyl ion). From the indications given by Letsinger, Maury, and Burwell (*J. Amer. Chem. Soc.*, 1951, **73**, 2373), fully active *sec.*-butyl chloride (from fully active *sec.*-butanol of $[\alpha]_D^{20}$ 15·1°, $[\alpha]_D^{25}$ 14·9°) would have $[\alpha]_D^{25}$ about 36·8°. On this basis, the *sec.*-butyl chloride produced in the pyrolysis was about 40% racemized, indicating that the "unimolecular" reaction occurred to at least this extent.



(III)

sec.-Butyl γ-chlorobutyrate, which might provide a model for the lactonization behaviour of poly-(*sec.*-butyl α-chloroacrylate), was stable when boiled by itself or in presence of hydrogen chloride, but readily evolved butene, hydrogen chloride, and *sec.*-butyl chloride when heated with very small amounts of zinc chloride, stannic chloride, or sulphuric acid. The *sec.*-butyl chloride produced from active *sec.*-butyl γ-chlorobutyrate was inverted in configuration, and showed activity (when corrected to initial *sec.*-butanol of the same rotatory power) similar to that produced in the pyrolysis of poly-[(+)-*sec.*-butyl α-chloroacrylate]. The kind of catalyst effective in bringing about the decomposition of the chlorobutyrate suggests that this was facilitated by formation at the carbobutoxy-group of an oxonium adduct with the catalyst. The formation of such an adduct would not of necessity imply the subsequent formation of free butyl ion.

If the chlorobutyrate is a model for the polychloroacrylate in its pyrolytic behaviour, hydrogen chloride is not a catalyst for the decomposition of the latter. Since no other possible catalyst is known to have been present in the polychloroacrylate, its decomposition may have been purely thermally induced.

Experimental

(+)-sec.-*Butyl α-Chloroacrylate.*—Technical (±)-*sec.*-butanol was purified by fractional distillation and resolved by Pickard and Kenyon's method (*J.*, 1913, **103**, 1937); the active alcohol had b. p. 98—99°, d_4^{20} 0·8079, $[\alpha]_D^{20}$ +15·1°.

α-Chloroacrylic acid was prepared from trichloroethylene by Crawford and McLeish's method (B.P. 514,619); it was purified by recrystallization from hot light petroleum, the solution being cooled to −15° before the crystals of acid were filtered off. These were freed from residual solvent *in vacuo* over calcium chloride and active charcoal.

Butanol (47 g.), chloroacrylic acid (80 g., 1·14 mol.), benzene (150 g.), 98% sulphuric acid (1 g.), and technical *tert.*-butylcatechol (1 g.) were mixed with shaking in the order named, and esterification carried out in an apparatus with automatic separation of water of reaction from the condensed reflux of benzene–water azeotrope. The reaction was complete in 6½ hours. The reaction mixture was cooled and made alkaline with potassium carbonate solution, and the organic layer washed twice with water and dried (Na_2SO_4), to give 227 g. of liquid. This was distilled under reduced pressure through a 9" Vigreux column. 69 G. of ester were obtained, of b. p. 56—59·5°/13 mm., n_D^{20} 1·4368. Redistilled in the same apparatus, 61·5 g. (59·6%) of ester were collected between 56·5° and 57°/13 mm. This had n_D^{20} 1·4368, d_4^{20} 1·0488, d_4^{25} 1·0424, $[R_L]_D$ 40·57 (Calc.: 40·58), $[\alpha]_D^{22}$ +34·2° (Found: Cl, 21·8. Calc. for $C_7H_{11}O_2Cl$: Cl, 21·8%).

Poly-[(+)-sec.-*butyl α-Chloroacrylate*].—The monomeric ester had been prepared some 15 hours previously, and had been stored in the dark at −15° to minimize autoxidation. Benzoyl peroxide (0·0125 g.) was dissolved in the ester (50 g.), and the solution poured into a casting cell, made of two sheets of glass separated by a flexible gasket round the edges. The size of the glass plates and thickness of the gasket were chosen to provide a sheet of the polymer of

3 mm. thickness. The cell was sealed up by replacing the gasket where it had been pulled out to allow of filling, and heated at 50° for 64 hours, by which time the ester had polymerized to a solid. A further 24 hours' heating at 100° was given to complete polymerization to equilibrium. On removal of the gasket and cooling, the resin separated from the glass plates. The polymer was glassy, clear, and colourless, and had n_D^{20} 1·4961, d_4^{20} 1·231, d_4^{26} 1·228, $[\alpha]_D^{21\cdot5}$ (solid) +8·0°, $[\alpha]_D^{21}$ (in chloroform, c = 2·290) +14·4°, (in methylene dichloride, c = 1·933) +13·7° (Found: Cl, 21·7%).

The polymer was coarsely powdered for pyrolysis experiments. This was done by chilling it in liquid nitrogen, which embrittled it so that it could readily be pulverized in a mortar whilst cold. The powder was dried *in vacuo* over phosphoric oxide.

Pyrolysis of Poly-[(+)-sec.-*butyl* α-*Chloroacrylate*].—The polymer was pyrolysed *in vacuo* (10^{-4} mm.) at 190°. The pyrolysis vessel was similar in construction to a " drying pistol " and the pyrolysis chamber was heated by the vapour of boiling ethylene glycol in the surrounding jacket. The polymer was contained in a glass tray of semicircular cross-section, fitting closely to the walls of the pyrolysis chamber, and measuring 13 cm. long by 2 cm. external diameter of cross-section. Each charge of polymer weighed approximately 10 g.; four pyrolyses were carried out.

The pyrolysis chamber was connected with a receiver which could be cooled in liquid nitrogen. The products of pyrolysis condensed here at any time could be distilled into a second receiver, also cooled in nitrogen, and graduated so that the volume of condensate could be measured. This second receiver could be isolated from the evacuated pyrolysis system, and the contents distilled at atmospheric pressure from baths of appropriate temperatures. It was proposed by this means to estimate the contents of the distillate in hydrogen chloride, butene, and crude butyl chloride, the last being the residue left when the condensate had reached room temperature. The method failed mainly because hydrogen chloride was retained by the condensate far above the b. p. of the former. Data obtained in the four pyrolyses are given below:

Polymer, g.	Pyrolysis residue, g.	Residue / Polymer, %	Cl content of residue, %	Crude butyl chloride (g.), after heating for (hours): 0—½	½—1	1—1½	1½—3½	Total
10·044	5·230	52·10	10·7	—	—	—	—	2·43
9·368	5·081	54·24	11·2	—	0·37	0·05	0·0	
8·899	4·864	54·67	11·4	0·29	0·47	0·13	0·01	0·90
8·756	4·769	54·46	11·4	0·51	0·34	0·07	0·10	1·02
38·077	19·944							4·35

Distillation of Crude sec.-*Butyl Chloride*.—The crude chloride (3·87 g.) was distilled from a small bulb sealed to a Vigreux column 15 cm. long and of 0·7-cm. bore. Butene and hydrogen chloride were at first evolved; condensation of slightly moist butyl chloride (0·39 g.) commenced at 55°; pure butyl chloride passed over at 68° (0·85 g.). A high-boiling residue remained (1·52 g.). The butyl chloride fraction had d_4^{20} 0·8693, d_4^{25} 0·8690, $[\alpha]_D^{21}$ −22·2°, $[\alpha]_D^{25}$ (in *n*-heptane, c = 2·802), −20° (Found: Cl, 37·7, 38·2. Calc. for C_4H_9Cl: Cl, 38·3%). (In these and other micro-Carius determinations of chlorine in butyl chloride, difficulty was found in sealing up the volatile chloride without loss.) The high-boiling residue had d_4^{20} 1·0128, d_4^{25} 1·0103, $[\alpha]_D^{21\cdot5}$ +15·4° (Found: Cl, 24·4%).

Properties of Pyrolysis Residue.—The sintered, light brown residue was insoluble in hot or cold water. It dissolved in cold dilute sodium hydroxide to a yellow, viscous solution; it did not dissolve in epichlorohydrin, tetrahydrofuran, acetone, dioxan, ethanol, methylene dichloride, or chloroform.

sec.-*Butyl* γ-*Chlorobutyrate*.—γ-*Chlorobutyric acid*. Tetramethylene chlorohydrin was prepared from tetrahydrofuran and hydrogen chloride (*Org. Synth.*, Coll. Vol. II, p. 571) and oxidized with nitric acid in the same way as described (*op. cit.*, Coll. Vol. I, 2nd Edn., p. 168) for oxidation of trimethylene chlorohydrin to β-chloropropionic acid, with molar substitution of tetramethylene chlorohydrin. The temperature of the oxidation mixture was allowed to rise to 50—55°. Tetramethylene chlorohydrin (505 g.) gave distilled γ-chlorobutyric acid (392 g.), b. p. 68—74°/0·8 mm.; on redistillation this gave 373 g. (65·5%) of acid, b. p. 67°/0·5 mm., m. p. 14°, n_D^{20} 1·4540, d_4^{20} 1·2373, $[R_L]_D$ 26·84 (Calc.: 27·08) (Found: Cl, 29·2. Calc. for $C_4H_7O_2Cl$: Cl, 28·95%).

Esterification with sec.-*butanol*. *sec.*-Butanol (37 g.), γ-chlorobutyric acid (65 g., 1·05 mol.), benzene (150 g.), and toluene-*p*-sulphonic acid hydrate (1·0 g.) were mixed and heated under

reflux in an apparatus provided with an automatic separator of water of esterification, until no more water was rejected. The reaction mixture was washed with water, made alkaline with 20% aqueous sodium hydroxide, washed again with water, and dried (Na_2SO_4). Solvent was removed, and the ester fractionated under reduced pressure, with use of a 9-in. Vigreux column. From (+)-*sec.*-butanol, d_4^{20} 0·8084, $[\alpha]_D^{20}$ +12·2°, the ester (34 g., 38%) was collected at 85—86°/10 mm., and had n_D^{20} 1·4323, d_4^{20} 1·0210, d_4^{25} 1·0156, $[R_L]_D$ 45·40 (Calc.: 45·67), $[\alpha]_D^{20}$ +17·9° (Found: Cl, 20·2. Calc. for $C_8H_{15}O_2Cl$: Cl, 19·85%). From (±)-*sec.*-butanol, the ester (30 g., 33·6%) had b. p. 84·5—85°/10 mm., n_D^{20} 1·4323, d_4^{20} 1·0207, $[R_L]_D$ 45·42 (Found: Cl, 20·4%).

(±)-sec.-*Butyl α-Chloropropionate*.—This was prepared similarly to the γ-chlorobutyrate. α-Chloropropionic acid (108·5 g.) gave redistilled ester (116·5 g., 70·8%), with b. p. 61·5°/15 mm., n_D^{20} 1·4201, d_4^{20} 1·0190, $[R_L]_D$ 40·88 (Calc.: 41·05) (Found: Cl, 21·8. Calc. for $C_7H_{13}O_2Cl$: Cl, 21·6%).

Pyrolysis of sec.-*Butyl γ-Chlorobutyrate*.—(*a*) The ester was contained in a 150-c.c. flask, provided with a thermometer reaching into the liquid, a narrow inlet tube for hydrogen chloride, and a 6-in. Vigreux column connected directly to a trap cooled to −80° in solid carbon dioxide–methanol. The flask was heated by a metal-bath. The ester (22 g.) was distilled at atmospheric pressure for 30 minutes without producing low-boiling material or evolving hydrogen chloride; the temperature of the boiling liquid was in the range 200—211°. A stream of dry hydrogen chloride was passed through for 45 minutes, the temperature of the boiling liquid being in the same range. It was estimated that about 5 molar proportions of hydrogen chloride passed through the boiling ester. On conclusion of this treatment, the trap contained only a drop of liquid, smelling of the ester.

(*b*) The above treatment of ester with hydrogen chloride at the b. p. was carried out with (±)-*sec.*-butyl hexanoate and α-chloropropionate. The temperatures of the liquid esters, and times of treatment were respectively 185—190°, 4 hours; and 173°, 2 hours. In both cases the sole condensate was a drop of liquid smelling of ester.

(*c*) Samples of ester containing in solution small amounts of zinc chloride, stannic chloride, or sulphuric acid began to evolve hydrogen chloride and butene at about 132°. Trimethylamine hydrochloride and aniline hydrochloride were not catalysts for this decomposition. Aluminium chloride caused more profound decomposition, with blackening.

(*d*) (+)-*sec.*-Butyl γ-chlorobutyrate (20 g.), containing in solution fused zinc chloride (0·05 g.), was heated in the apparatus used in (*a*). At ester temperature 130°, decomposition commenced, with evolution of hydrogen chloride. Between 142° and 169°, distillation occurred, with a vapour temperature at the column top ranging between 39° and 60°, the temperature falling with time. The pyrolysis occupied 55 minutes, after which distillation practically ceased. The residue weighed 11·5 g. (Found: Cl, 10·9%). The distillate (9 g. at −80°) weighed 6·5 g. when warmed to room temperature, the loss in weight being due to evolution of hydrogen chloride and butene. It was distilled through a 6-in. Vigreux column. Distillation commenced at 68°. After neglect of a small forerun (0·2 g.), the butyl chloride (3·4 g.) was collected at 68°. The residue (<0·5 g.) was mainly column drainings. The butyl chloride had d_4^{20} 0·866, $[\alpha]_D^{20}$ −16·0° (Found: Cl, 38·0. Calc. for C_4H_9Cl: Cl, 38·3%).

The pyrolysis residue was treated with an equal volume of water, to extract butyrolactone, and the extract evaporated on the water-bath. This residue was converted into γ-hydroxybutyrophenylhydrazide by heating it at 100° with phenylhydrazine. The solid product, crystallized from chloroform, and recrystallized from benzene, had m. p. 93—93·5°. Seib (*Ber.*, 1927, **60**, 1399) gives 93·7—94° for the m. p. of this compound.

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861. *Dimethylberyllium. Part I. Vapour Pressure and Vapour-phase Association.*

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The vapour pressure of dimethylberyllium has been measured between 100° and 180°, and the vapour density between 160° and 200°. The extrapolated sublimation temperature is 217°. From a study of the pressure dependence of the vapour density it is concluded that the vapour contains monomer, dimer, trimer, for which structures are proposed, and higher polymers, the last only becoming important under near-saturation conditions. Heat and entropy terms have been obtained for the monomer–dimer and the monomer–trimer equilibria. The significance of the apparent heat of sublimation is discussed in the light of the association equilibria, and the heat of sublimation of the solid polymer into monomer is deduced.

The energy difference between two half bonds and one whole bond is 9—12 kcal., depending on the degree of polymerisation; this is compared with the value of 10 kcal. for the similar quantity in trimethylaluminium and its dimer. The entropy change on dimerisation is discussed in relation to the use of 3*d* orbitals by carbon in compounds of this type.

The dialkyl derivatives of beryllium present structural and valency problems similar to those which have developed from the study of the alkyls and hydrides of its neighbours in the Periodic Table, *viz.*, lithium, boron, aluminium, and gallium. Very few organoberyllium compounds have been properly characterised, but all of these have properties which preclude their formulation as salts and indicate covalent but polymeric structures. For example, dimethylberyllium (Gilman and Schulze, *J.*, 1927, 2663) is a white crystalline solid, sublimation temperature 217°/760 mm., and diethyl- (Goubeau and Rodewald, *Z. anorg. Chem.*, 1949, **258**, 162) and di*iso*propyl-beryllium (Coates and Glockling, unpublished) are colourless, rather viscous * liquids which may be distilled slowly in a high vacuum at room temperature. Since these compounds are covalently saturated in their monomeric forms, any polymerisation involving the formation of additional covalent bonds requires their classification as electron-deficient molecules, *i.e.*, the total number of electrons available for valency-bond formation is less than twice the minimum number of bonds required to hold any reasonable structure together. Other examples of electron-deficient molecules are ethyl-lithium, m. p. 95° to a non-conducting liquid, which may easily be distilled in a high vacuum and is strongly associated in benzene solution (Hein, Petzchner, Wagler, and Segitz, *ibid.*, 1924, **141**, 161), all the hydrides of boron, trimethylaluminium which is dimeric (Pitzer and Gutowsky, *J. Amer. Chem. Soc.*, 1946, **68**, 2204; Rundle, *ibid.*, 1947, **69**, 1327), and digallane Ga_2H_6 (Wiberg and Johannsen, *Angew. Chem.*, 1942, **55**, 38).

A recent *X*-ray analysis (Snow and Rundle, *Acta Cryst.*, 1951, **4**, 348) has shown that solid dimethylberyllium has a polymeric structure similar to that of silicon disulphide, beryllium and methyl groups replacing silicon and sulphur respectively. All the beryllium–carbon bonds are equivalent, with an approximately tetrahedral distribution of methyl groups round each beryllium atom; one of the most significant features of the structure is the small Be–C–Be angle (66°), which will be mentioned again below. In the present work we have investigated the nature of gaseous dimethylberyllium which is also associated, the heat of sublimation of monomer from the solid, and the heat of formation of dimer and trimer from monomer, by means of vapour-pressure and vapour-density measurements.

Experimental

Dimethylberyllium.—For both vapour-pressure and vapour-density measurements the preparative method of Burg and Schlesinger (*J. Amer. Chem. Soc.*, 1940, **62**, 3425) was preferred to the Grignard method of Gilman and Schulze (*loc. cit.*), since ether co-ordinates to dimethylberyllium and it was found that samples prepared by high-vacuum sublimation of the solid

* Their viscosity is of the same order as that of concentrated sulphuric acid.

obtained from ethereal solution had somewhat higher vapour pressures, particularly at lower temperatures, than samples obtained from metallic beryllium and dimethylmercury (*e.g.*, 1·6 and 0·6 mm. respectively at 100°). Burg and Schlesinger's method was modified slightly in that beryllium powder was found to react faster than small lumps of metal, and instead of being heated in a sealed tube the reactants were refluxed together under slightly greater than atmospheric pressure in an apparatus sealed to a vacuum-system. In a typical preparation beryllium powder (1 g.) was placed in the reaction tube, which was then sealed into the vacuum-system and pumped and baked out at 400°; dimethylmercury (4·3 ml.) was condensed on the beryllium, the apparatus filled with oxygen-free dry nitrogen to atmospheric pressure, and the mixture refluxed for 36 hours, whereafter very little dimethylmercury remained. The residue of it was removed *in vacuo* at room temperature and the dimethylberyllium was then sublimed *in vacuo* from any excess of metal. The light metal is readily carried by a stream of dimethylberyllium vapour, but was easily separated by means of a small, grade 3, sintered disc sealed into the apparatus. This method gave a product which was slightly contaminated with metallic mercury, which could not be removed by sublimation over gold foil since the latter parts with mercury even at the lowest temperatures (about 100°) at which the alkyl may be sublimed. For vapour-pressure and vapour-density measurements the presence of mercury does not matter since its vapour pressure is accurately known and appropriate corrections were included. For experiments (particularly some of those described in Parts II and III) in which it was necessary to weigh samples of dimethylberyllium, the presence of mercury was serious while a trace of ether did not matter; in such cases the sample was dissolved in pure dry ether and either filtered through a sintered disc or, more conveniently, siphoned from the residual mercury. These operations were all carried out in the vacuum-apparatus with rigorous exclusion of oxygen and water vapour, both of which react with dimethylberyllium with considerable vigour.

Vapour Pressure and Vapour Density.—These measurements were carried out in the " high-temperature bulb " of known volume, described by Burg and Schlesinger (*ibid.*, 1937, **59**, 780) and by Sanderson (" The Vacuum Manipulation of Volatile Compounds," Wiley, 1948); the bulb was immersed in an oil-thermostat containing a resistance thermometer connected to an a.c. bridge thermo-regulator (Coates, *J. Sci. Instr.*, 1944, **21**, 86). Temperatures were measured by standardised mercury thermometers reading to tenths of a degree. Vapour-density measurements required accurate determination of the quantity of dimethylberyllium present in the high-temperature bulb; these quantities were determined, not by weighing (on account of mercury contamination and the small weights involved), but by hydrolysis after each experiment, and removal of the liberated methane by a Töpler pump through a liquid-oxygen trap into a gas-burette. The direct hydrolysis of dimethylberyllium is so vigorous and exothermic that some carbon, hydrogen, and other products are sometimes formed; therefore it was moderated by first adding a slight excess of trimethylamine, which formed a less reactive co-ordination compound (see Part II), and then water. Vapour densities were not measured above 200° since thermal decomposition then becomes quite appreciable, and is shown by the deposition of colourless glistening crystals unlike dimethylberyllium in appearance, a decrease of pressure, and a residual pressure on cooling to room temperature after an experiment.

Results

Vapour Pressure.—Over the temperature range studied, 100—180°, the plot of log p against temp.$^{-1}$ (K) was not quite linear, but the observed vapour pressures are represented closely by two linear equations:

$$100\text{—}155^\circ : \log_{10} p_{\text{mm.}} = 12{\cdot}530 - 4771/T$$

$$155\text{—}180^\circ : \log_{10} p_{\text{mm.}} = 13{\cdot}292 - 5100/T$$

Observed vapour pressures are compared in Table 1 with those calculated from the above equations.

TABLE 1.

Temp. (c)	100·2°	115·0°	125·4°	130·2°	135·1°	140·6°	145·3°
$p_{\text{obs.}}$	0·62	1·72	3·39	4·98	6·81	9·82	13·1
$p_{\text{calc.}}$	0·56	1·71	3·59	4·98	6·92	9·89	13·3
Temp. (c)	151·5°	155°	160°	165°	170°	175°	180°
$p_{\text{obs.}}$	19·8	24·4	33·1	45·1	61·0	82·4	110·0
$p_{\text{calc.}}$	19·8	24·2	33·2	45·1	61·1	82·0	109·9

Vapour-phase Association.—Preliminary experiments having indicated a degree of association between 1 and 2 under conveniently accessible conditions of temperature and pressure, it was

clear that monomeric dimethylberyllium was present in the vapour. It was then necessary to decide whether the equilibrium involved dimeric or trimeric molecules or both; this was done by calculating equilibrium constants K_D and K_T on the respective assumptions of monomer–dimer and monomer–trimer equilibria, where

$$K_D \text{ (atm.}^{-1}) = p_{\text{dimer}}/p^2_{\text{monomer}}$$

and

$$K_T \text{ (atm.}^{-2}) = p_{\text{trimer}}/p^3_{\text{monomer}}$$

Eight series of vapour-density determination were carried out with quantities of dimethylberyllium from 1·26N-c.c. (*i.e.*, c.c. calculated as monomer at N.T.P.) to 27·3N-c.c., pressure readings being taken at 5° intervals from about 10° above the temperature at which all the solid disappeared to 200°. In this way it was possible to examine the variation of K_D and K_T with pressure at any chosen constant temperature, the latter in practice being restricted to 160° to 200°. Table 2 indicates that K_D slowly increases with pressure, while K_T rapidly diminishes;

TABLE 2. *Variation of* K_D *and* K_T *with pressure at* 190° C.

$p_{mm.}$	25	31	52	81	101	151
K_D (atm.$^{-1}$)	4·4	4·6	4·8	5·5	6·2	6·6
K_T (atm.$^{-2}$)	0·62	0·51	0·28	0·20	0·17	0·11

thus it follows that the equilibrium primarily involves monomer and dimer but that some trimer is also present. Hydrogen cyanide behaves in much the same way (Giauque and Rührwein, *J. Amer. Chem. Soc.*, 1939, **61**, 2626), the association being due to hydrogen bonding. The present probem was solved by making the same assumption that led to the solution of the hydrogen cyanide case, namely, that as the pressure approaches zero the trimer equilibrium becomes negligible, hence the true dimer constant for any temperature may be obtained by plotting the apparent K_D (as given in Table 2 for 190°) against p and extrapolating to $p = 0$. In this way the values of K_D (true) given in Table 3 were obtained.

The values of K_T were calculated as follows. Let x^{-1} = mean degree of association of the vapour; then $x = PV/\boldsymbol{R}T(1 + \lambda P)$. The compressibility factor λ, if taken as equal to that of hydrogen chloride (M for HCl = 36·5; M for Me_2Be = 39·1), has an insignificant effect on the results over the temperature and pressure range investigated, and was therefore ignored. Let α = fraction of the dimethylberyllium present in dimeric form, and let β = fraction in trimeric form; then the fraction of the dimethylberyllium in the monomeric form is $1 - \alpha - \beta$, and $x = 1 - \alpha/2 - 2\beta/3$.

Since

$$p_{\text{monomer}} = p \cdot \frac{1 - \alpha - \beta}{1 - \alpha/2 - 2\beta/3} = p \cdot \frac{1 - \alpha - \beta}{x}$$

and

$$p_{\text{dimer}} = p \cdot \frac{\alpha/2}{1 - \alpha/2 - 2\beta/3} = p \cdot \frac{\alpha}{2x}$$

then

$$pK_D(\text{true}) = \alpha x/2(1 - \alpha - \beta)^2 = 2\alpha x/(3x - 1 - \alpha/2)^2$$

The solution to this equation is

$$\frac{\alpha}{2} = \frac{8x}{q} + 3x - 1 - 4\sqrt{\frac{x}{q}\left(\frac{4x}{q} + 3x - 1\right)}$$

where $q = 4pK_D$ (true). Since K_D (true) has been found as described above, it is now possible to calculate α for experimentally observed values of temperature and pressure, and hence $\beta(=1 - 3x - \alpha/2)$. Then, since

$$p_{\text{trimer}} = p \cdot \frac{\beta/3}{1 - \alpha/2 - 2\beta/3} = p \cdot \frac{\beta}{3x}$$

$$p^2K_T = \beta x^2/3(1 - \alpha - \beta)^3$$

Value of α, β, and K_T were calculated for a pressure of 0·1 atm. from 170° to 200°.

At much lower pressures the values of β are so small that accuracy is poor, and at higher pressures the available temperature range is limited by the vapour pressure of dimethylberyllium. Even at 170° the value of x had to be obtained by a short extrapolation, since the vapour pressure of dimethylberyllium at 170° is only 0·08 atm. The results are given in Table 3.

TABLE 3.

Temp. (c)	K_D (true, atm.$^{-1}$)	K_T (atm.$^{-2}$) *	α *	β *	Temp. (c)	K_D (true, atm.$^{-1}$)	K_T (atm.$^{-2}$) *	α *	β *
170°	12·3	52	0·48	0·16	190°	3·7	6·1	0·338	0·063
175	9·1	29	0·454	0·132	195	2·8	3·6	0·298	0·045
180	6·7	21	0·408	0·126	200	2·1	2·4	0·256	0·036
185	4·9	11	0·376	0·090					

* $p = 0{\cdot}1$ atm.

The values of β at the lower temperatures suggest that a small amount of tetramer is likely to be present; consequently the true values of K_T should be obtained by determining K_T as above for various pressures and extrapolating to zero pressure, but in fact the experimental restrictions (the vapour pressure at lower temperatures and thermal decomposition above 200°) did not allow this. The temperature dependence of K_D (true) and K_T is given by

$$\log_{10} K_D \text{ (true)} = 10{\cdot}92 - 532_5/T$$

and

$$\log_{10} K_T = 20{\cdot}3 - 977_0/T,$$

hence

$$\Delta H_D^\circ = -24{\cdot}4 \pm 1 \text{ kcal. per mole of dimer,}$$

$$\Delta G_D^\circ = -24400 + 50T \text{ cal.,}$$

$$\Delta S_D^\circ = -50 \pm 2 \text{ cal. per mole of dimer per degree;}$$

and

$$\Delta H_T^\circ = -44{\cdot}7 \pm 5 \text{ kcal. per mole of trimer,}$$

$$\Delta G_T^\circ = -44700 + 93T \text{ cal., and}$$

$$\Delta S_T^\circ = -93 \pm 10 \text{ cal. per mole of trimer per degree.}$$

Latent Heat of Sublimation.—Table 3 shows that at 174°, when the vapour pressure of dimethylberyllium is 0·1 atm., the vapour consists of about 14% of trimer, 46% of dimer and 40% of monomer. At other temperatures of saturated vapour the composition will clearly be different. Since the heats of association (given above) are quite large it is at first sight rather surprising that the logarithm of the vapour pressure is so nearly a linear function of T^{-1}. From the vapour pressure equation given above, for the temperature range 155—180° (over which the equilibrium data may be considered applicable), let $R\mathrm{d}\log_e p/\mathrm{d}(1/T) = \Delta H_s' = 23{\cdot}3$. This may be regarded as an apparent heat of sublimation; it is, in fact, the quantity of heat, in kcal., required to obtain one mole of vapour *of mean molecular weight* M/x from the solid, where M is the molecular weight of monomeric dimethylberyllium. Then the heat required to obtain x moles of vapour is $\Delta H_s' . x$, but this amount of vapour contains $\alpha/2$ moles of dimer and $\beta/3$ moles of trimer. The heat required to convert $x = (1 - \alpha/2 - 2\beta/3)$ moles of mixed vapour into one mole of monomeric vapour is $-\Delta H_D . \alpha/2 - \Delta H_T . \beta/3$; hence the heat required to obtain one mole of monomeric vapour from the solid, which may be regarded as the true heat of sublimation ΔH_s, is given by

$$\Delta H_s = \Delta H_s'(1 - \alpha/2 - 2\beta/3) - \Delta H_D . \alpha/2 - \Delta H_T . \beta/3.$$

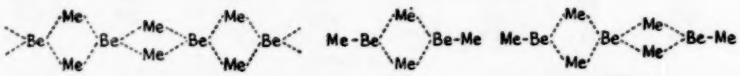
It is apparent that since $\Delta H_s' \approx -\Delta H_D \approx -\frac{1}{2}\Delta H_T$, $\Delta H_s \approx \Delta H_s'$. From the expressions for K_D and K_T given above, it follows that

$$\frac{2\beta}{3\alpha} \cdot \frac{(1 - \alpha/2 - 2\beta/3)}{1 - \alpha - \beta} = \frac{K_T . p}{K_D} \text{ and } \frac{4\beta}{3\alpha^2}(1 - \alpha - \beta) = K_T/K_D^2$$

By solving these equations for α and β at various temperatures and pressures equal to the corresponding vapour pressures, the relation between the true and the apparent heat of sublimation may be examined more closely. The composition of the saturated vapour at 180°, calculated in this way, is 41% of monomer, 44% of dimer, and 14% of trimer, whence $\Delta H_s = 23{\cdot}4_8$ kcal. per mole of monomer. The results for 160° are 27% of monomer, 50% of dimer, and 23% of trimer, whence $\Delta H_s = 23{\cdot}4_6$. Clearly ΔH_s, which can be taken as $23{\cdot}5 \pm 1$ kcal., is constant well within the accuracy with which $\Delta H_s'$ and the other data were measured, and, secondly, the high proportion of trimer at 160° indicates that tetramer and doubtless still higher polymers are present to an increasing extent at lower temperatures.

Discussion

In view of the structure (I) of solid dimethylberyllium (Snow and Rundle, *loc. cit.*), in which broken lines represent half bonds, the following structures for the dimer (II) and trimer (III) present in the vapour would seem to be highly probable :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Me

$I' = 426$, and $I'' = 572 \times 10^{-40}$ g. cm.^{2}. Although it is highly probably that the end-methyl groups in the dimer can rotate freely, the matter of free rotation or a fixed configuration for the bridge-methyl groups is less easy to decide and is of considerable significance in view of the recent theory of Gillespie (*J.*, 1952, 1002) concerning the use of 3*d* orbitals by carbon in this type of compound. According to this theory the bridge-methyl groups should be fixed, whereas if the molecular orbital forming the Be–C–Be bond is derived from a carbon sp^3 tetrahedral orbital there appears to be no reason why the methyl groups should not rotate freely since steric interference would be very small. The rotational entropy is therefore calculated for the two situations, (*a*) fixed bridge-methyl groups, and (*b*) freely rotating bridge-methyl groups. In the former the symmetry number of the dimer is $4 \times 3^2 = 36$, and by the method given by Aston (Taylor and Glasstone, "A Treatise on Physical Chemistry," Vol. I, Van Nostrand, 1942), the rotational entropy at 180°, $S_r(a) = 33{\cdot}9$ e.u. In the latter case the symmetry number is $4 \times 3^4 = 324$, the number of rotational degrees of freedom is seven instead of five, and at 180° $S_r(b) = 42{\cdot}0$ e.u. From these results and the experimental value for the total internal entropy change on dimerisation (13 ± 2 e.u.), the quantity (vibrational entropy of the dimer $- 2 \times$ vibrational entropy of the monomer) becomes $0{\cdot}3 \pm 2$ e.u. on situation (*a*) and $-7{\cdot}8 \pm 2$ e.u. on situation (*b*). Since the number of bonds in the dimer is necessarily more than twice that in the monomer, and some of them must be half-bonds with relatively low force constants, it appears inevitable that the vibrational entropy of the dimer should be more than twice that of the monomer. Hence it is concluded (1) that the observed entropy change is reasonably consistent with the proposed structures, and (2) that, in support of the theory of Gillespie, the bridge-methyl groups are more likely to be fixed than free to rotate. This type of approach appears to provide one of the very few ways by which Gillespie's theory can be tested. Accurate equilibrium and calorimetric entropy data on trimethylaluminium (which is simpler to deal with experimentally than dimethylberyllium) are much to be desired in this connection.

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THE UNIVERSITY, BRISTOL. [*Received, June 30th*, 1952.]

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862. *Dimethylberyllium. Part II.* Co-ordination Compounds.*

By G. E. COATES and N. D. HUCK.

Dimethylberyllium forms co-ordination compounds with trimethylamine, trimethylphosphine, and dimethyl and diethyl ether, but not with trimethylarsine or dimethyl sulphide. The properties of these indicate that the order of stability of the compounds is N > P > O. Whereas the co-ordination affinity of trimethylamine to dimethylberyllium is more than sufficient to break down the polymeric structure of the latter, forming the volatile substance $Me_2\overset{-}{B}e\text{–}\overset{+}{N}Me_3$, there is evidence to show that weaker donor molecules such as trimethylphosphine have a co-ordination affinity similar in magnitude to the affinity of dimethylberyllium molecules for each other; the latter situation results in the formation of a number of co-ordination compounds with various Be : P ratios, and in some rather peculiar properties shown by dimethylberyllium–trimethylphosphine and –dimethyl ether systems. The formation of an unstable compound $(Me_2Be)_2(NMe_3)_3$ has been demonstrated; this is interpreted on the basis of half-bonding between one nitrogen and two beryllium atoms.

THE strongly electron-deficient nature of dimethylberyllium (see Part I *) should permit the formation of a series of stable co-ordination compounds, for example, with the donor elements of Groups V and VI of the Periodic Table. In this respect dimethylberyllium

* Part I, preceding paper.

might be expected to behave like trimethylaluminium (Brown and Davidson, *J. Amer. Chem. Soc.*, 1942, **64**, 316) and trimethylgallium (Coates, *J.*, 1951, 2003), which form 1 : 1 co-ordination compounds, $Me_3\bar{A}l\text{–}\dot{P}Me_3$ being a typical example. In fact, however, the situation is very much more complex with dimethylberyllium, which forms more than one compound with each donor molecule with which it combines. This paper is concerned only with donor molecules containing no reactive hydrogen atom, since donor molecules such as alcohols and secondary amines react with dimethylberyllium to form methane and associated hydroxy- or amino-beryllium compounds which will be the subject of Part III. The donor molecules studied were trimethylamine, trimethylphosphine, trimethylarsine, dimethyl and diethyl ether, and dimethyl sulphide.

Experimental

All the experiments were conducted in a high-vacuum apparatus of standard design. Materials were prepared and purified as described in Part I of this series and in Part I of the trimethylgallium series (Coates, *loc. cit.*). Dimethylberyllium, prepared from metallic beryllium and dimethylmercury, was separated from mercury by solution in dry ether followed by filtration through a grade-4 sintered disk and subsequent removal of ether in a high vacuum. Most of the co-ordination equilibria were studied in the " high-temperature bulb " (Burg and Schlesinger, *J. Amer. Chem. Soc.*, 1937, **59**, 780; Sanderson, " The Vacuum Manipulation of Volatile Compounds," Wiley, 1948). For convenience, quantities of materials used in experiments are usually given in normal c.c. (N-c.c.), *i.e.*, the volume which the (monomeric) vapour would occupy at N.T.P.

Trimethylamine.—Dimethylberyllium–trimethylamine. Dimethylberyllium (about 180N-c.c.) was sublimed into a reaction bulb and cooled in liquid oxygen. Trimethylamine (238N-c.c.) was condensed on the dimethylberyllium, and the reaction bulb allowed to warm to room temperature; the ensuing reaction was quite mild since no visible change was observed. The excess of trimethylamine (64N-c.c.; v. p. 678 mm. at 0°) was passed through a trap cooled to −60° and collected at −183°; thus 174N-c.c. had reacted. A little of the white crystalline product had condensed in the trap cooled to −60°, but most remained in the reaction vessel; it was distilled into a number of small sample bulbs cooled in liquid oxygen and sealed. On slow cooling of the warm *product*, large colourless rhombic crystals, m. p. 36°, were formed, which reacted vigorously with air and moisture, forming dense white clouds of beryllium oxide and hydroxide and liberating trimethylamine.

The contents (0·2301 g.) of one of the sample bulbs were cautiously hydrolysed by water, followed by hydrogen chloride, in the vacuum apparatus. Methane (identified by vapour pressure, 105·2 N-c.c.) was pumped into a gas burette through a liquid-oxygen trap by means of a Töpler pump, and the trimethylamine (0·1373 g.) was estimated by distillation into standard acid in the usual way [Me_2Be,NMe_3 (0·2301 g.) requires CH_4, 105·0N-c.c.; NMe_3, 0·1385 g.].

The vapour pressure, given for various temperatures in Table 1, cannot be represented by any simple equation of the type, $\log_{10}p = -A/T + B$, since the slope of the log p–T^{-1} graph varies with temperature in the sense that the apparent latent heat of vaporisation decreases much more rapidly than usual with increasing temperature. No decomposition occurred during these measurements. The vapour pressure of the solid corresponds to a latent heat of sublimation of 20 ± 1 kcal./mole, that of the liquid corresponds to a latent heat of evaporation of about 12 kcal./mole at 50° and about 8 at 130°. The molecular weights, from measurement

Table 1.

Temp. (c)	26°	30°	32°	36°	42°	48°	56°	64°
V. p. (mm.)	1·34 *	1·83 *	2·65 *	3·92 *	5·7	8·1	12·5	18·4
Temp. (c)	72°	80°	90°	100°	110°	120°	130°	140° †
V. p. (mm.)	26·2	36·6	53·7	76·6	101·2	137·4	178·5	222·0

* Solid. † Sample volatilised completely at higher temps.

of the temperature and pressure of a known weight (0·1395 g.) in the high-temperature bulb, are given in Table 2. The compound is thus monomeric at higher temperatures, but shows signs of association.

Table 2.

Temp. (c)	150°	155°	160°	170°	180°
M	105·3	104·5	103·7	102·1	100·5
Degree of association	1·073	1·065	1·056	1·040	1·024

Bisdimethylberyllium–tristrimethylamine. Dimethylberyllium–trimethylamine (14·20N-c.c.) was condensed in the high-temperature bulb (182·2 c.c.) and followed by trimethylamine (15·84N-c.c.). The gas pressure in the bulb was measured between −30° and +170°; reproducible results were obtained with both heating and cooling. In Fig. 1 the volume of the gaseous contents of the bulb, reduced to N-c.c., is plotted against temperature (for one experiment). From −30° to +27° the bulb contained solid and gas only. From −30° to +9·4° the gas pressure followed Charles's law, *i.e.*, the volume reduced to N-c.c. was constant (8·80N-c.c.). Since the total quantity of trimethylamine in the system was 14·20 + 15·84 = 30·04N-c.c., it follows that the solid phase contained 14·20N-c.c. of dimethylberyllium combined with 30·04 − 8·80 = 21·24N-c.c. of trimethylamine. The ratio of trimethylamine to dimethylberyllium in the solid phase was therefore 1 : 21·24/14·20, or 1 : $1{\cdot}49_6$, and the formula of the solid $(Me_2Be)_2(NMe_3)_3$. On heating from lower temperatures there was a very sudden increase of pressure at 9—10° followed at about 27° by melting of the solid; this was not sharp, since some evolution of trimethylamine from the compound $(Me_2Be)_2(NMe_3)_3$ had already occurred. The

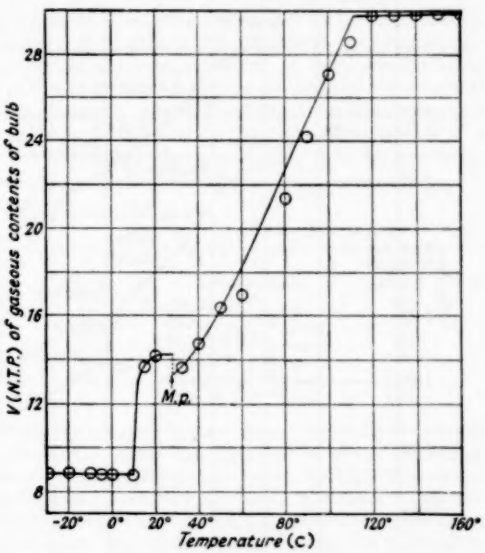


FIG. 1. Me_2Be,NMe_3 (14·2N-c.c.) + NMe_3 (15·8N-c.c.).

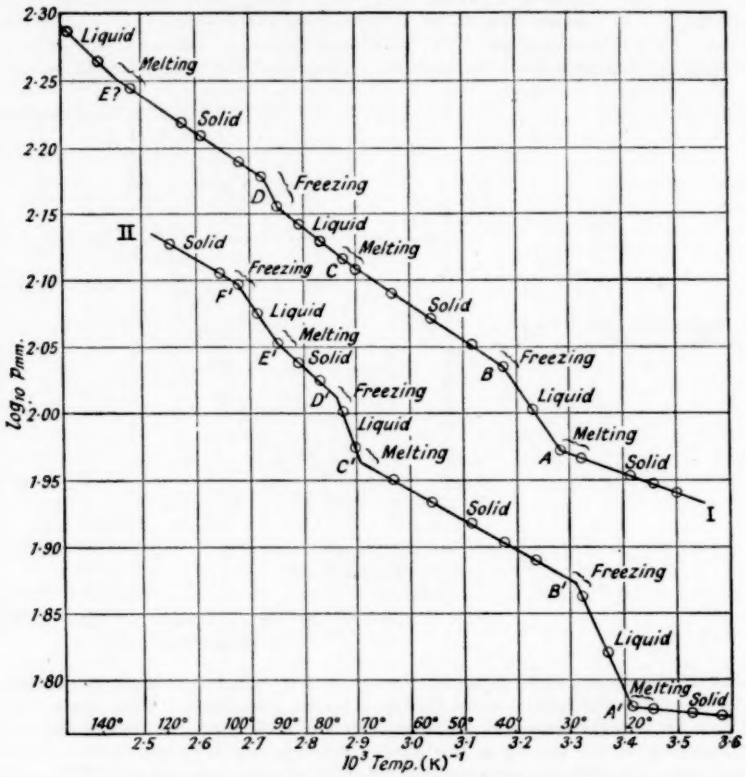
melting was always accompanied by a slight pressure drop which is a strong indication that the extra molecule of trimethylamine is not held as a lattice compound. With increasing temperature the pressure steadily increased, owing both to the further dissociation of the (now liquid) 2 : 3 compound and to the vaporisation of the 1 : 1 compound, until from 120° to 170° the contents of the bulb were entirely gaseous and of constant volume (reduced to N.T.P.) of 29·9N-c.c. This corresponds within experimental error (including deviations from the simple gas law) to 14·20N-c.c. of Me_2Be,NMe_3 originally introduced, together with the 15·84N-c.c. of trimethylamine added.

Trimethylphosphine.—Interaction with trimethylphosphine was much more complicated. Preliminary experiments showed that trimethylphosphine is a weaker donor toward dimethylberyllium than is trimethylamine; at room temperature, at which dimethylberyllium is virtually non-volatile, all the trimethylphosphine could be separated by pumping in a high vacuum. However, it was evident from measurements of the amounts of trimethylphosphine present in the condensed state (at pressures well below the saturation pressure of trimethylphosphine vapour) that a considerable range of compounds $(Me_2Be)_x(PMe_3)_y$ is formed, each one being stable only in a certain range of temperature and pressure of trimethylphosphine.

The results of two typical experiments are shown graphically in Fig. 2 (I and II). For the first of these, dimethylberyllium (3·79N-c.c., this quantity, being too small to weigh accurately, was determined from the volume of methane, 7·58 ± 0·05N-c.c., liberated on hydrolysis at the conclusion of the experiments) was transferred to the high-temperature bulb and an excess of

trimethylphosphine (24·0N-c.c.) was added. As the mixture warmed from −183° no reaction was observed until about −25° when colourless rhombic crystals slowly formed from the original fine white needles of dimethylberyllium, liquid trimethylphosphine being present at this temperature. The variation of pressure with temperature on continued heating to 160° is shown in Fig. 2 (I), in which $\log_{10}$ pressure (mm.) is plotted against (temp., K)$^{-1}$ × 10^3. This form of representation is preferred since it shows the characteristic discontinuities better than others, and both a dissociation equilibrium and, over a limited temperature range, the change of pressure of gas with temperature, give an approximately linear relation between log p and T^{-1} [in fact, for Charles's law, d log p/d(1/T) = $-T$]. Pressure changes were followed both on

FIG. 2.



Dimethylberyllium (3·79N-c.c.) + (I) *trimethylphosphine* (24·0N-c.c.).
" " + (II) *trimethylphosphine* (18·5N-c.c.).

heating and cooling; equilibrium was established rather slowly, and a single (heating) run usually took 11—12 hours. Equilibrium on cooling was attained even more slowly, and since the same phenomena were then observed in the reverse order, the latter data are not recorded in detail.

The crystalline solid which formed at ~ −25° melted at 27—31°, with a subsequent rapid pressure increase. The composition of this solid [Fig. 2 (I), point A] was $Me_2Be(PMe_3)_2$, since the volume of the gaseous contents of the bulb was 16·4N-c.c., so 24·0—16·4 = 7·6N-c.c. of trimethylphosphine were combined with 3·79N-c.c. of dimethylberyllium. The composition of the solid was very nearly constant at a Be : P ratio of 1 : 2 from temperatures near the condensation point of trimethylphosphine to point A. The increase of slope of the plot must be due to the decomposition of this compound with evolution of trimethylphosphine. As the temperature was increased the liquid gradually froze again, becoming completely solid just below

50°, when its composition (point *B*, from the volume of gaseous trimethylphosphine) was $(Me_2Be)_2(PMe_3)_3$. At this point the rate of increase of pressure with temperature suddenly decreased. This new solid melted at about 70—75° when there was another change of slope; at this stage, point *C*, the composition of the condensed phase was approximately Me_2Be,PMe_3. This, however, provides hardly any evidence for the existence of a 1 : 1 compound; the latter, however, is more clearly indicated in Fig. 3 and was definitely proved by experiments at constant temperature mentioned below. Between 90° and 95° the liquid froze again, and when it became completely solid (point *D*), its composition was $Me_2Be(PMe_3)_{0\cdot63}$, *i.e.*, corresponding to an empirical formula $(Me_2Be)_3(PMe_3)_2$. At these higher temperatures it may not be justifiable to neglect the vapour pressure of the co-ordination compounds themselves, although these are likely to be small compared with the total pressure (100—200 mm.) of trimethylphosphine present. The third solid, $(Me_2Be)_3(PMe_3)_2$, melted rather gradually between 130° and 140° and the liquid finally crystallised again at 160°. In these last stages the volume of combined trimethylphosphine is so small (of the order of 1 c.c.) and the vapour pressure even of dimethylberyllium becomes quite appreciable (*e.g.*, 10 mm. at 140°) that it is not possible to follow the composition of the condensed phase.

Fig. 2 (II) refers to an experiment in which a smaller proportion of trimethylphosphine is present; at any temperature the pressure of the latter is less than in the experiment to which Fig. 2 (I) refers, and the changes of slope are more pronounced. A very similar sequence of events occurred, but the points *A'*, *B'*, *C'*, and *D'* corresponding to those of Fig. 2 are at lower temperatures, showing that the lower dissociation pressures of the successive compounds are reached at lower temperatures, as would be expected, and further inflections, points *E'* and *F'*, were observed. The compositions of the condensed phase, assuming it to be non-volatile, for these points are given in Table 3.

TABLE 3.

	Fig. 2 (I)			Fig. 2 (II)		
Point	Composition	Pressure (mm.)	Temp.	Composition	Pressure (mm.)	Temp.
A, *A'*	$Me_2Be(PMe_3)_{3\cdot01}$	94	32°	$Me_2Be(PMe_3)_{3\cdot00}$	60	20°
B, *B'*	$(Me_2Be)_3(PMe_3)_{2\cdot00}$	108	42	$(Me_2Be)_3(PMe_3)_{2\cdot94}$	74	29
C, *C'*	$Me_2Be(PMe_3)_{1\cdot05}$	131	75	$Me_2Be(PMe_3)_{1\cdot08}$	93	70
D, *D'*	$(Me_2Be)_3(PMe_3)_{1\cdot89}$	148	94	$(Me_2Be)_3(PMe_3)_{2\cdot04}$	106	80
E'	—	—	—	$(Me_2Be)_4(PMe_3)_{2\cdot09}$	112	90
F'	—	—	—	$(Me_2Be)_5(PMe_3)_{1\cdot84}$	120	104

Some attempts were made to establish the composition of these compounds by experiments at constant temperature and variable pressure. Again the composition of the condensed phase was determined from the total amount of trimethylphosphine put in the high-temperature bulb less the N.T.P. volume of trimethylphosphine vapour at any given pressure. This procedure was also complicated by the melting or freezing of the condensed phase which occurred under some conditions when the pressure was altered. Moreover, the time taken for the establishment of equilibrium, particularly with a solid phase, was excessive. However, from isotherms at 25° and 50° the existence of the compounds Me_2Be,PMe_3 and $(Me_2Be)_3(PMe_3)_2$ was definitely demonstrated since the composition of the solid remained constant in these instances over quite a wide range of pressure. The 25° isotherm gave a dissociation pressure of 5·5 mm. for the 1 : 1, and 80—82 mm. for the 2 : 3 compound.

In view of the uncertainties mentioned above, and the smaller inflections observed at higher temperatures, considerably less reliance should be placed on the formulæ of the compounds containing the smaller ratios of phosphorus to beryllium, but at least the first four compounds of Table 3 appear quite definite. The observed succession of melting and freezing over the entire temperature range studied does, however, very strongly suggest that a series of compounds is formed: $Me_2Be(PMe_3)_2$, $(Me_2Be)_2(PMe_3)_3$, Me_2Be,PMe_3 or $(Me_2Be)_2(PMe_3)_2$, $(Me_2Be)_3(PMe_3)_2$, $(Me_2Be)_4(PMe_3)_2$, and $(Me_2Be)_5(PMe_3)_2$.

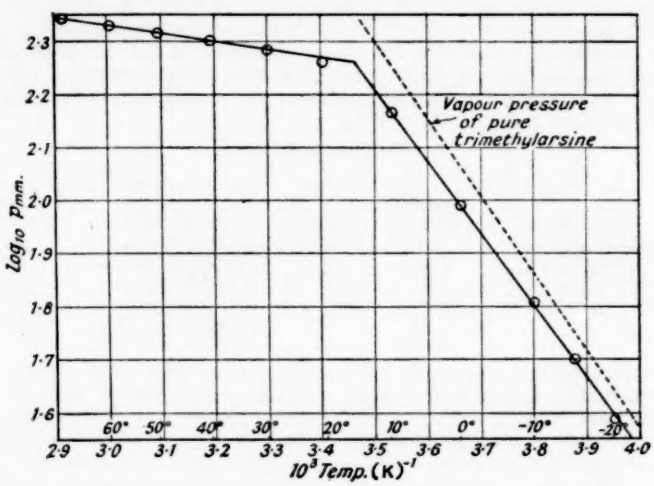
At low temperatures (−20° to −38°) and at pressures below the saturation pressure of trimethylphosphine, so that liquid trimethylphosphine was present, the vapour pressure observed was less than that of the pure phosphine since it contained some dissolved co-ordination compound, no doubt $Me_2Be(PMe_3)_2$.

Trimethylarsine.—Dimethylberyllium (21·0N-c.c.) and trimethylarsine (42·5N-c.c.) were condensed in the high-temperature bulb. No reaction appeared to take place, except that dimethylberyllium seemed to dissolve slightly in the arsine. As long as liquid trimethylarsine was present the pressure (Fig. 3) was slightly below the vapour pressure of pure trimethylarsine.

as would be expected if some dimethylberyllium was dissolved in it. At higher temperatures the variation of pressure with temperature followed the gas law, and the volume of gas present was 42·0 N-c.c., indicating no combination with the solid dimethylberyllium.

Dimethyl Ether.—The reaction between dimethylberyllium and an excess of dimethyl ether took place when the high-temperature bulb warmed to 5°, whereupon the former slowly liquefied. On cooling, the liquid product formed transparent crystals, which, in several experiments, began to melt at 5·0—5·5°, with sudden increase of pressure, and became entirely liquid at 9—10°. Two such experiments are represented in Fig. 4, in which plot I refers to a system containing 10·4N-c.c. of dimethylberyllium and 48·1N-c.c. of dimethyl ether, and for II the quantities were 14·3 and 65·6 respectively. In no case was the composition of the solid (m. p. 5—10°) constant; it varied between $Me_2Be(OMe_2)_{1\cdot68}$ and $Me_2Be(OMe_2)_{1\cdot8}$. This contrasts with the experiments with trimethylphosphine, in which the composition of the solid formed at low temperatures was always very close to the ratio 1 : 2. The composition of the liquid obtained on melting this solid (points *A* and *A'*) was, however, always close to $(Me_2Be)_2(OMe_2)_3$. On further heating, this liquid gradually dissociated until its composition, points *B* and *B'*, was $Me_2Be_2OMe_2$, and then decomposed into its components, points *C* and *C'*, without any sign of the formation of

FIG. 3. *Dimethylberyllium* (21·0N-c.c.) + *trimethylarsine* (42·5N-c.c.).



compounds with a higher Be : O ratio. At lower pressures of dimethyl ether such compounds are formed. Fig. 5 represents two experiments in which 24·5N-c.c. of dimethylberyllium and 48·9N-c.c. (plot I) and 23·0N-c.c. (plot II) of dimethyl ether were present. In plot I the composition of the solid stable from −3° down to −30° or below, point *A* and to the right (measurements could not be made at much lower temperatures since the mercury would freeze), was constant at $Me_2Be(OMe_2)_{0\cdot98}$, *i.e.*, a 1 : 1 compound within experimental error. This began to decompose above −5° and melted between 10° and 15° with evolution of dimethyl ether; decomposition continued until the composition of the liquid was close to $(Me_2Be)_2OMe_2$; at 43° (point *B*) the liquid was suddenly transformed into solid dimethylberyllium with evolution of all the dimethyl ether (the volume of gas then being 48N-c.c., point *C* and to the left).

In plot II (23·0N-c.c. OMe_2) the condensed phase was solid at all temperatures. Over the temperature range −5° to +10° the volume of gas present was constant at 14·9N-c.c. (point *D* and to the right); thus 23·0—14·9 or 8·1N-c.c. of dimethyl ether were combined with 24·5N-c.c. of dimethylberyllium; thus the composition of the solid was $(Me_2Be)_3OMe_2$, or, as discussed below, more probably $(Me_2Be)_6(OMe_2)_2$. This compound began to decompose abruptly at 17° and above 30° (point *E* and to the left) the bulb contained only solid dimethylberyllium and gaseous dimethyl ether (23·0N-c.c.). The slope of the linear part of plot II corresponds to a heat of dissociation of approximately 9 kcal. per mole of dimethyl ether.

The compositions of the condensed phases represented by *A*, *B*, *C*, *A'*, *B'*, *C'* on Fig. 4 and *A*, *B*, *D* on Fig. 5, and corresponding temperatures and pressures, are given in Table 4. From

these results it appears that the compounds $(Me_2Be)_2(OMe_2)_3$, Me_2Be,OMe_2, $(Me_2Be)_3OMe_2$, and $(Me_2Be)_3OMe_2$ are formed. These are much less stable than the trimethylphosphine compounds since they dissociate at considerably lower temperatures.

FIG. 4. *Dimethylberyllium and dimethyl ether.*

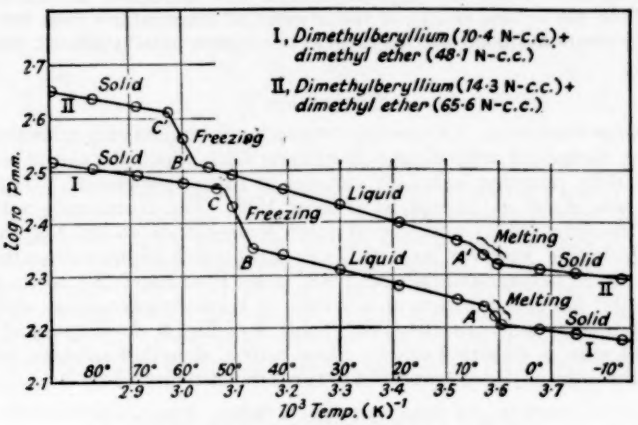
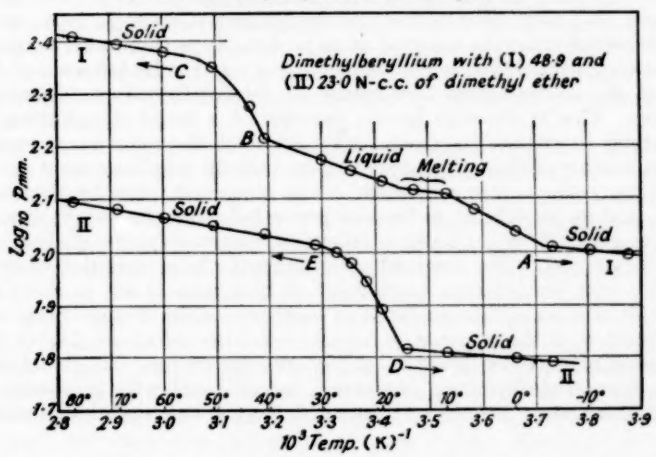


FIG. 5. *Dimethylberyllium and dimethyl ether.*



Diethyl Ether.—A smaller number of experiments was carried out with diethyl ether. At low temperatures, when liquid ether was present, its vapour pressure was somewhat less than that of pure ether on account of the solution of dimethylberyllium–ether complexes in the liquid. At higher temperatures and at pressures below the saturation pressure of ether, solid gradually separated as the temperature rose, with steady evolution of ether into the gas phase. In one

TABLE 4.

FIG. 4				FIG. 5			
Point	Composition	Pressure (mm.)	Temp.	Point	Composition	Pressure (mm.)	Temp.
A	$(Me_2Be)_2(OMe)_{2\cdot98}$	172	6°	*A*	$Me_2Be(OMe_2)_{0\cdot98}$	102	−3°
A′	$(Me_2Be)_2(OMe_2)_{3\cdot10}$	231	11	*B*	$(Me_2Be)_2(OMe_2)_{1\cdot07}$	164	43
B	$Me_2Be(OMe_2)_{1\cdot01}$	224	46	*D*	$(Me_2Be)_{3\cdot01}OMe_2$	65	17
B′	$Me_2Be(OMe_2)_{2\cdot98}$	326	57				
C	$(Me_2Be)_n$	290	52				
C′	$(Me_2Be)_n$	410	63				

experiment with 19·5N-c.c. of dimethylberyllium and 39·1N-c.c. of diethyl ether, the condensed phase was solid from 20° to just over 40°, the solid then suddenly decomposing to dimethylberyllium, with an increase in pressure from 127 to 173 mm. over a 5° temperature range. There was no indication of the formation of compounds of definite composition.

Dimethyl Sulphide.—When the high-temperature bulb contained dimethylberyllium and dimethyl sulphide, the volume (N-c.c.) of the latter at all temperatures from 20° (pressure 163 mm.) to 110° (pressure 217 mm.) was the same as the volume initially added; thus no reaction took place.

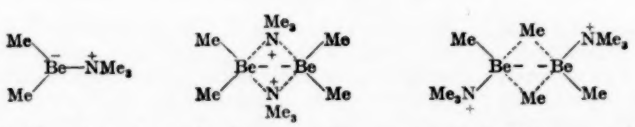
Discussion

Relative Donor Properties.—Of the donor compounds studied only trimethylamine gave a co-ordination compound with dimethylberyllium from which the donor molecule could not be removed by pumping in a high vacuum at room temperature. This compound, Me_2Be,NMe_3, was stable as vapour to at least 180°. The compounds with trimethylphosphine all decomposed on pumping at room temperature, so did the dimethyl ether complexes; the former, however, were stable to considerably higher temperatures than the latter. Thus the 2 : 1 compound $(Me_2Be)_2PMe_3$, point *E'* of Fig. 2 (II), melts and begins to decompose at 90° under a pressure of 112 mm. of trimethylphosphine, while the corresponding oxygen compound $(Me_2Be)_2OMe_2$, point *B* of Fig. 5, decomposes at 43° under a pressure of 164 mm. of dimethyl ether. Since neither dimethyl sulphide nor trimethylarsine reacts, the order of donor properties towards dimethylberyllium is:

$$NMe_3 > PMe_3 > OMe_2 > AsMe_3, SMe_2 = 0.$$

This order is the same as that found with trimethylaluminium (Brown and Davidson, *J. Amer. Chem. Soc.*, 1942, **64**, 316) and trimethylgallium (Coates, *J.*, 1951, 2003); it is the order to be expected when the acceptor atom is of the type that forms simple co-ordinate links without complication due to double bonding or any similar influence of *d* orbitals.

Nature of the Co-ordination Compounds of Dimethylberyllium.—Dimethylberyllium–trimethylamine. This is the only known example of a metal co-ordination compound, sufficiently stable to exist in the gaseous state, in which the metal has the rather unusual co-ordination number of *three*. One may assume that the beryllium atom assumes the sp^2 orbital grouping, giving a planar molecule. The compound might be dimeric in the condensed state, and its insolubility in benzene prevented molecular-weight measurements in solution (other, generally either donor or otherwise reactive solvents, are best avoided with this class of substance). The observed quite unusually large variation of its latent heat of vaporisation with temperature, from about 12 kcal./mole at 50° to about 8 at 130° is, however, a hint that an equilibrium such as monomer ⇌ dimer may obtain in the liquid, and is consistent with the presence of a high proportion of dimer (higher L_V) at lower temperatures and of monomer (lower L_V) at higher temperatures. The structure of the solid dimethylberyllium–trimethylamine compound, which could only be resolved by *X*-ray analysis, is thus a matter of some interest, since there are at least three reasonable possibilities, *viz.*,

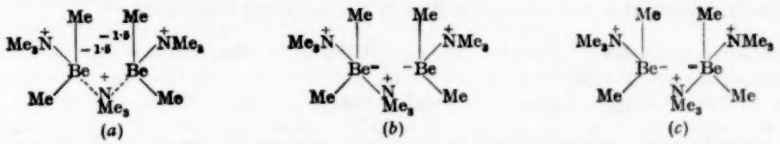


In these and other formulæ, a broken line has an exact significance and represents a half-bond.

Bisdimethylberyllium–tristrimethylamine. This compound was not obtained as a gas, so it is not certain that it is monomeric. It is, however, difficult to see how it could be associated. The nature of the bonding in it is rather obscure, but one possibility is that two Me_2Be,NMe_3 units are bonded together by means of one trimethylamine molecule. The general chemistry of beryllium reveals a very strong tendency towards the formation of four tetrahedrally disposed covalent bonds; this is illustrated, for example, by the BeF_4^{--} ion, basic beryllium acetate, and the beryllium acetylacetone compound. The same

tendency manifests itself in solid dimethylberyllium (see Part I and below), an electron-deficient structure in which the beryllium forms essentially four half-bonds.

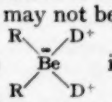
It is now suggested that a somewhat similar type of bonding is present in the compound $(Me_2Be)_2(NMe_3)_3$:



(*a*) (*b*) (*c*)

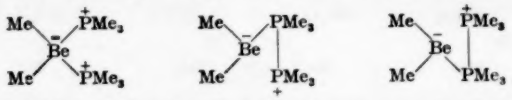
Structure (*a*) is regarded as equivalent to the two " resonance " forms (*b*) and (*c*), but is preferred. The formal charges on the beryllium and nitrogen atoms would correspond to complete symmetry of the molecular orbitals, *i.e.*, each bond having no bond dipole moment. Differences of electronegativity would, of course, reduce these charges by a molecular-orbital asymmetry in the sense of a greater electron density at the more electronegative (*i.e.*, C or N) end of each bond to beryllium. The Be–N–Be bond is regarded as consisting of one molecular orbital, doubly occupied, derived from one tetrahedral orbital from each beryllium atom and one from the central nitrogen atom, just as the B–H–B bond in diborane is generally regarded as derived from one tetrahedral orbital from each boron and one 1*s* hydrogen orbital.

The main objections to this proposed structure are (*a*) that it would seem difficult, on stereochemical grounds, for the beryllium atoms to approach sufficiently close to the nitrogen atom, which must be fairly obstructed by the three methyl groups, although it must be remembered that half bonds are substantially longer than whole bonds, and (*b*) that this would be the only example of nitrogen with a co-ordination number of five.* In this class of compound, however, there is ample evidence that carbon can attain this co-ordination number, and Gillespie (*J.*, 1952, 1002) has suggested on theoretical grounds that nitrogen may possibly do likewise.

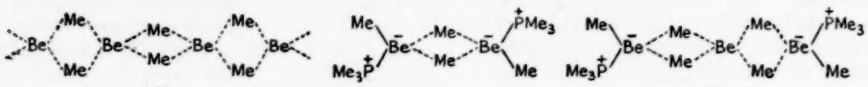
The trimethylphosphine compounds. There is clear evidence for the formation of compounds with Be : P ratios of 1 : 2, 2 : 3, 1 : 1, and 3 : 2, with somewhat less reliable evidence for the formulæ of compounds with higher Be : P ratios, but little doubt as to their existence. In one way the simplest to interpret is the 1 : 2 compound $Me_2Be(PMe_3)_2$, since this represents beryllium achieving its stable co-ordination number of four without any need to invoke half-bonds. On the other hand, one must enquire why such a compound was not formed by trimethylamine, which is a considerably stronger donor molecule. It may possibly have been due to wrong experimental conditions, but this is unlikely since the compound $(Me_2Be)_2(NMe_3)_3$ persisted down to −30° in the presence of free trimethylamine. The failure to prepare a compound $Me_2Be(NMe_3)_2$ is unlikely to be due to steric interference between the trimethylamine molecules—such interference would be even greater in the bistrimethylphosphine compound, and moreover the compound $Me_3C{\cdot}CMe_2{\cdot}CMe_3$, which should have much the same size and shape, is quite stable. Beryllium is a relatively electropositive element (electronegativity 1·5 on the Pauling scale) and may not be able to combine with two donor molecules forming a compound of structure  in which D represents a donor molecule, unless the atoms bonded to beryllium are so electronegative that the resulting polarity of the bonds effectively removes much of this double negative charge from the beryllium atom. This would be so in the case of the numerous co-ordination compounds of beryllium chloride of the type Cl_2BeD_2 (reviewed by Sidgwick, " The Chemical Elements and Their Compounds," Oxford Univ. Press, 1950, pp. 208—213), chlorine being a highly electronegative element; in the case of dimethylberyllium, where R = Me, the atoms bonded to the beryllium may not be sufficiently electronegative. The problem then takes the form of why a 1 : 2 compound $Me_2Be(PMe_3)_2$ is obtained, particularly since phosphorus is a less electronegative element than nitrogen. Now one of the more

* The authors are indebted to a Referee for these points.

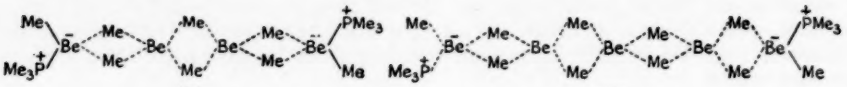
important differences between phosphorus and nitrogen is that the maximum covalency of the former is not limited to four, and it is tentatively suggested that, just as the P–O bond in phosphine oxides is less polar than the N–O bond in amine oxides owing to the possibility of a covalency of five for phosphorus, $R_3P{=}O$, the compound dimethylberyllium –bistrimethylphosphine may be represented by the following structures:



For there to be appreciable P–P bonding it would be necessary for the P–Be–P angle to be somewhat less than 109°. The second and third of the above structures would not be



(A) (B) (C)



(D) (E)

possible with nitrogen or oxygen as donor atoms, and it will be recalled that no compound $Me_2Be(OMe_2)_2$ was obtained.

The existence of the remaining compounds, *viz.*, $(Me_2Be)_3(PMe_3)_2$, $(Me_2Be)_2PMe_3$, and $(Me_2Be)_5(PMe_3)_2$, becomes intelligible on recalling the structure (*A*) of dimethylberyllium itself, since donor molecules would provide a very simple means for ending this polymeric chain. Therefore it is suggested that these compounds and probably also the 1 : 1 complex have the constitutions (*B*—*E*). The compound $(Me_2Be)_2PMe_3$ may in this way be regarded as $(Me_2Be)_4(PMe_3)_2$, but there may be some doubt about the 1 : 1 compound, for which, as for the other trimethylphosphine complexes, there is no evidence of molecular weight. It may have the above structure, or it may be monomeric like the trimethylamine compound $Me_2Be{\leftarrow}NMe_3$, but evidence in favour of the dimeric formula is presented later.

Ether compounds. The observed compounds formed by dimethyl ether are consistent with the views set out above. No bisether complex could be obtained; this could be due either to the weaker donor character of dimethyl ether than of trimethylphosphine, or to the reasons (applicable equally to ether) advanced to show why no bistrimethylamine compound was formed, or to both these reasons. The compounds $(Me_2Be)_2(OMe_2)_3$, Me_2Be,OMe_2, $(Me_2Be)_2OMe_2$, and $(Me_2Be)_3OMe_2$ are regarded as similar to the analogous trimethylphosphine compounds.

Heats of Co-ordination.—It is possible to make approximate estimates of the heat of formation of co-ordinate bonds to beryllium. Reaction (1) occurs spontaneously at room temperature, and the dissociation pressure of trimethylamine was quite undetectable and may be considered as less than 10^{-4} atmosphere. Hence the free-energy change $\Delta G_1^\circ < -5{\cdot}5$ kcal./mole. Since the major part of the entropy change, ΔS_1°, must be due to the

$$Me_2Be(s,\ polymer) + NMe_3(g) \longrightarrow Me_2Be,NMe_3(s) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
$$Me_2Be(s,\ polymer) \longrightarrow Me_2Be(g,\ monomer) \quad . \quad . \quad . \quad . \quad . \quad (2)$$
$$Me_2Be,NMe_3(s) \longrightarrow Me_2Be,NMe_3(g) \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$
$$Me_2Be(g,\ monomer) + NMe_3(g) \longrightarrow Me_2Be,NMe_3(g) \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

disappearance of the translational entropy of a mole of trimethylamine, which is 38 e.u. at 25° and 1 atm., one may conclude that $\Delta S_1 \approx -40$. Hence ΔH_1 must be $< -(5{\cdot}5 - 40) \times 300$ or $< -17{\cdot}5$ kcal./mole. Since $\Delta H_2 = 23{\cdot}5 \pm 2$ kcal./mole of monomer (from Part I, but there is some uncertainty about extrapolation to room temperature from 150—180°, at which ΔH_2 was measured), and $\Delta H_3 = 20 \pm 1$ (this paper), it follows that $\Delta H_4 = \Delta H_1 + \Delta H_3 - \Delta H_2 < -21 \pm 3$. The corresponding heat terms for the co-ordination of

trimethylamine to trimethylboron (Brown and Gerstein, *J. Amer. Chem. Soc.*, 1950, **72**, 2923) and trimethylgallium (Coates, unpublished observation) are −17·6 and −21·0 kcal./mole respectively. Trimethylaluminium–trimethylamine (Brown and Davidson, *loc. cit.*) was too stable to permit measurement of dissociation equilibria, therefore $\Delta H < -21$ kcal., as for the beryllium compound discussed above. Hence it appears that the relative acceptor properties of these elements are in the order B < Ga < Al,Be.

The dissociation pressure of $(Me_2Be)_2(NMe_3)_3$, for which a half-bonded structure has been suggested, appears to be somewhat less than 0·1 atm. at 25°, hence $\Delta G°$ for the reaction $(Me_2Be)_2(NMe_3)_3 \longrightarrow 2Me_2Be,NMe_3 + NMe_3$ is $\sim +(1—2)$ kcal./mole. When similar assumptions (as above) are made about the entropy change, ΔH becomes about −14 kcal./mole; thus the heat of co-ordination of one mole of trimethylamine to two moles of Me_2Be,NMe_3, by—it is suggested—two half-bonds, is of the order of 14 kcal.

From Fig. 2 and Table 3 it appears that the dissociation pressures for equilibria of the type

$$(n + 1)(Me_2Be)_n(PMe_3)_2 \rightleftharpoons n(Me_2Be)_{n+1}(PMe_3)_2 + 2PMe_3$$

where $n = 3$, 4, or 5, are of the order of 100 mm. at 80°. Thus $\Delta G° \approx 1$ kcal./mole of PMe_3, and, when similar assumptions are made for $\Delta S°$, $\Delta H° \approx -15$. On the basis of the structures, proposed above, of these compounds, $\Delta H°$ would be roughly the heat of co-ordination of one trimethylphosphine molecule to the dimethylberyllium polymer, less the heat required to convert two beryllium–carbon half-bonds into one whole bond. The latter quantity was estimated in Part I as about 11 kcal. for short polymers, hence the required heat of co-ordination is approximately 26 kcal./mole of PMe_3. A similar calculation based on the observed dissociation pressure of $(Me_2Be)_2(PMe_3)_2$, 5·5 mm. at 25°, leads to an identical value for the heat of co-ordination. It is interesting that, if the above compound is regarded as Me_2Be,PMe_3, a value of ~ 58 kcal. is obtained for the heat of co-ordination; this impossible value provides evidence in favour of the dimeric structure, a conclusion which cannot be altered unless wildly improbable entropy changes for the solids are assumed.

Although dimethyl sulphide forms quite a stable co-ordination compound with trimethylaluminium ($\Delta H = -19$ kcal./mole; Brown and Davidson, *loc. cit.*), it does not react with dimethylberyllium. On the supposition that the heat of co-ordination of dimethyl sulphide to dimethylberyllium is the same as to trimethylaluminium, a reversal of the type of calculation given above leads to a dissociation pressure of 200—300 atmospheres for the dimethylberyllium–dimethyl sulphide system (a result in agreement with the reported failure to observe such compounds).

Although dimethylberyllium is undoubtedly a very strong acceptor, as would be expected in view of the highly electron-deficient structure of the solid polymer, the formation of co-ordination compounds and their nature are highly sensitive to the heat of co-ordination. In conclusion, it appears that co-ordination compounds are formed only if the heat of co-ordination per mole of donor is at least 10—11 kcal. greater than the heat required to form one Be–C whole bond from two half-bonds, *i.e.*, >*ca.* 21—22 kcal. Thus we arrive at the following approximate estimate of heats of co-ordination to dimethylberyllium: S, As < 21; 21—22 < O < 25—26; P ~ 26; N > 26 kcal.

Finally, there appears to be only one parallel to the behaviour of dimethylberyllium with donor molecules. Stecher and Wiberg (*Ber.*, 1942, **75**, 2003) found that aluminium hydride, which clearly has a polymeric structure $(AlH_3)_n$ (Longuet-Higgins, *J.*, 1946, 139), reacts with trimethylamine in a complex manner. Slightly volatile mixed crystals of $AlH_3,NMe_3 + AlH_3,2NMe_3$ are described, from which were prepared, under suitable conditions of temperature and partial pressure of trimethylamine, compounds of approximate compositions AlH_3,NMe_3, $(AlH_3)_3,NMe_3$ and $(AlH_3)_5,NMe_3$. Thus the behaviour of trimethylamine with aluminium hydride appears to be intermediate in character between that of trimethylamine and trimethylphosphine towards dimethylberyllium.

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THE UNIVERSITY, BRISTOL. [*Received, June 30th*, 1952.]

863. *Dimethylberyllium. Part III.* Reactions with some Compounds containing Reactive Hydrogen.*

By G. E. Coates, F. Glockling, and N. D. Huck.

Dimethylberyllium reacts with methylamine, dimethylamine, dimethylphosphine, methyl alcohol, methanethiol, or hydrogen chloride, forming methane and di-, tri-, or poly-meric products. Dimethylamine affords a trimeric compound $(MeBe{\cdot}NMe_2)_3$, to which a cyclic structure (I) has been assigned. Methyl alcohol gives a dimeric methoxide $(MeBe{\cdot}OMe)_2$ (VII), which readily disproportionates to dimethylberyllium and beryllium dimethoxide. The other substances studied lead to involatile or but slightly volatile products of doubtless polymeric constitution.

Like Grignard reagents and other active organometallic compounds, dimethylberyllium reacts with substances containing even very weakly acidic hydrogen, *e.g.*, primary and secondary amines, and alcohols. In very few instances, however, have the primary products been isolated or characterised. We have investigated several such reactions and find the products to be polymeric.

Experimental

Preparations and most of the manipulations of the compounds described below were carried out in a high-vacuum apparatus. The reagents were prepared and purified as described in Part I of this series (*J.*, 1952, **4496**) and in Part I of the Trimethylgallium series (Coates, *J.*, 1951, 2003), with the exception of methanethiol, which was obtained by alkaline hydrolysis of methyl*iso*thiourea sulphate, the product being washed with dilute sulphuric acid, dried ($CaCl_2$), and fractionally condensed from a solution in dry propanol containing a little sodium propoxide. The v. p. of the product was 600 mm. at 0° (Davidson and Brown, *J. Amer. Chem. Soc.*, 1942, **64**, 316, give 601 mm.).

Compounds were not analysed but their compositions were established by quantitative synthesis, a procedure usual with this class of substance, since in working with a vacuum-apparatus nothing can be lost. Quantities are expressed as N-c.c. (c.c. reduced to N.T.P.).

cyclo-$\mu\mu'\mu''$*-Trisdimethylaminotrimethyltriberyllium* (I).—Dimethylamine (125·7 N-c.c.) was condensed on dimethylberyllium (56·5 N-c.c.); on warming to room temperature there was no visible reaction but only 68·7 N-c.c. of dimethylamine (v. p. 564 mm. at 0°) were recovered; hence 57·0 N-c.c. had reacted, to form a 1 : 1 addition compound. At room temperature the pressure in the reaction vessel increased very slowly, reaching 5 mm. (in a volume of 139·2 c.c.) after 4 hours. The reaction vessel was then slowly warmed, with a noticeable increase in the rate of gas evolution, until the compound melted at 44° with a vigorous evolution of gas. The mixture was then heated at 50° until gas evolution ceased, and the gas [identified as methane by its v. p. (83 mm. at −183°)] was transferred to a gas burette; 55·9 N-c.c. of methane were formed. Since 56·5 N-c.c. of dimethylberyllium reacted with 57·0 N-c.c. of dimethylamine and formed 55·9 N-c.c. of methane, the composition of the residue was $[BeNMe_2]_x$.

A larger quantity, prepared by the same method, was distributed among several sample tubes (for subsequent opening with a magnetic breaker) by distillation in a high vacuum. It was important to avoid overheating in this operation since thermal decomposition takes place rather easily with the formation of permanent gas and a non-volatile white residue.

The compound forms white crystals, m. p. 55—56°, which fume slowly in the air; it is rapidly hydrolysed by water. The v. p., from 60° to 100°, is given by the equation $\log_{10} p_{mm.} = 8{\cdot}605 - 2889/T$; hence the latent heat of vaporisation is 13·2 kcal./mole. Vapour-density measurements showed that a 63·2 mg. sample, equivalent to 20·8 N-c.c. of monomeric $MeBe{\cdot}NMe_2$ occupied a volume of 6·65 N-c.c. at 180° and 6·85 N-c.c. at 190°, corresponding to degrees of association of 3·13 and 3·04 respectively. Since some thermal decomposition takes place at these temperatures, the molecular weight was also measured with a Swiętoslawski differential ebulliometer (14-junction thermocouple) in carefully dried benzene [Found: *M*, 207·7 in 0·202% solution; 205·0 in 0·362% solution. $C_9H_{27}Be_3N_3$ requires *M*, 204·4]. The material is therefore cyclo-$\mu\mu'\mu''$*-trisdimethylaminotrimethyltriberyllium* (I).

* Part II, preceding paper.

Heating equimolar quantities of (I) with trimethylamine caused no change in volume (reduced to N-C.C.) between −20° and 50°, indicating absence of combination.

The thermal decomposition of (I) was examined by the prolonged heating of 7·8 N-C.C. at 180° until there was no further pressure change; a white solid of amorphous appearance was deposited and, on cooling, 3·5 N-C.C. of gas were removed and analysed by combustion (Found: CH_4, 98%; H_2, 2%).

Dry hydrogen chloride (120·7 N-C.C.) was condensed on (I) (9·8 N-C.C.), and the mixture allowed to warm to room temperature; no reaction appeared to take place. On slow heating, reaction began at 80° (decrease of pressure), and became quite rapid at higher temperatures. The reaction vessel was kept at 140° until the pressure was constant. The mixture was liquid at 140°, but gradually crystallised at room temperature. The residual gas consisted of hydrogen chloride (48·5 N-C.C.) and methane (9·8 N-C.C.); hence one mole of (I) had reacted with 7·4 moles of hydrogen chloride with the formation of one mole of methane.

Reaction of Dimethylberyllium with Methylamine.—Methylamine (36·7 N-C.C.) was condensed on dimethylberyllium (37·0 N-C.C.) at −183°. On gradual warming, a crystalline solid (III) appeared very soon after the methylamine melted (−90°), but almost immediately began to decompose with the evolution of gas and formation of a white amorphous solid (IV). When the temperature had reached 0° the gas evolution had practically ceased, and the pressure in the reaction vessel indicated that 16 N-C.C. of gas (identified as methane) had been formed; hence one mole of each reactant had produced slightly less than 0·5 mole of methane. On continued warming, the white solid melted at 10° with subsequent decomposition to form another white solid (V) and more methane. The reaction vessel was kept at 40° until the pressure was constant. The volatile contents were then pumped off (37·2 N-C.C.) and identified as methane (v. p. at −183°); hence one mole of methane had been formed from each mole of reactant. The non-volatile residue (V), when gradually heated, evolved gas very slowly at 80°. The decomposition became rapid at 110°, and was completed at 200°, 17·6 N-C.C. of methane being collected; hence a total of 54·8 N-C.C. of methane had been formed at this stage, *i.e.*, 1·47 moles per mole of dimethylberyllium. The residue (VI) evolved 14·1 N-C.C. of methane on hydrolysis; the total amount of methane produced was thus 68·7 N-C.C. (93% of the theoretical quantity for decomposition of all the dimethylberyllium).

cyclo-μμ′-*Dimethoxydimethyldiberyllium* (VII).—Methyl alcohol (56·1 N-C.C.) was condensed on dimethylberyllium (57·1 N-C.C.) at −183°; on slow warming a violent reaction was observed just after the methyl alcohol had melted. On reaching room temperature the gas formed in this reaction was pumped off (56·7 N-C.C.) and identified as methane by its v. p. at −183°. The residue in the reaction vessel consisted of a white solid and a colourless liquid; it became entirely liquid at 90°, and, on cooling, completely solidified to clear crystals (VII), m. p. 23—25°. The v. p. of this substance could not be measured since at >120° white solid appeared again and increased in quantity with increasing temperature. This effect was reversible but above 150° methane was irreversibly formed, so neither vapour pressures nor vapour densities were measured. The molecular weight was measured ebullioscopically in benzene (Found: *M* 103·6 in 0·159% solution; 112·0 in 0·265% solution. $C_4H_{12}O_2Be_2$ requires *M*, 110·2). cyclo-μμ′-*Dimethoxydimethyldiberyllium* reacts slowly with moist air and vigorously with water, forming methane and white clouds of beryllium hydroxide.

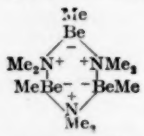
Reaction with Methanethiol.—Methanethiol (22·9 N-C.C.) was condensed on dimethylberyllium (22·7 N-C.C.) at −183°. When the mixture was allowed to warm to room temperature, reaction became rapid at about −10° but was much less vigorous than that with methyl alcohol. Methane (23·5 N-C.C.) was collected and the white solid residue heated to 100° to promote any rearrangement which might occur. No change was apparent and on cooling white needles suggestive of dimethylberyllium were visible. In a repetition of this experiment the volatile material formed by heating the primary product to 140° was sublimed out of the reaction vessel. This material absorbed trimethylamine, to give a volatile crystalline solid, m. p. 36°, and was therefore dimethylberyllium (dimethylberyllium–trimethylamine has m. p. 36°; Part II).

Methylberyllium Chloride.—Hydrogen chloride (26·8 N-C.C.) was condensed on dimethylberyllium (27·1 N-C.C.) at −183°; on warming, no reaction occurred below −5° since below this temperature the contents of the reaction vessel were always completely condensable in liquid oxygen. The reaction appeared to be complete after 1 hour's heating at 120—130°, and, on cooling, 26·7 N-C.C. of methane, containing no hydrogen chloride, were collected. The white residue therefore had the composition MeBeCl. The vapour pressure of this material, from 120° to 190°, is given by $\log_{10} p_{mm} = 6{\cdot}52 - 2614/T$ (p = 1 mm. at 128°).

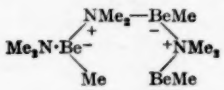
Discussion

The 1 : 1 co-ordination compound between dimethylberyllium and dimethylamine is probably very similar to the compound $Me_2\bar{B}e,\dot{N}Me_3$ described in Part II; the presence of a reactive hydrogen atom in the secondary amine renders it unstable, in contrast to the trimethylamine compound, and vigorous elimination of methane occurs at the low melting point (44°). The trimeric decomposition product very probably has a cyclic structure (I) like those assigned to some similar compounds of aluminium (Brown and Davidson, *loc. cit.*) and gallium (Coates, *loc. cit.*). The alternative, open-chain structure (II) is rejected since it contains a bicovalent beryllium atom and would be expected to co-ordinate with trimethylamine, which it does not. Further, no other example of a solid or liquid compound containing bicovalent beryllium is known.

The reaction between (I) and hydrogen chloride, in which only one mole of methane is formed from a mole of (I) with absorption of between 7 and 8 moles of hydrogen chloride, is



(I)



(II)

evidently much more complex than the reaction of the analogous aluminium compound (Brown and Davidson, *loc. cit.*)

$$(Me_2Al{\cdot}NMe_2)_2 + 8HCl = 2Me_2\dot{N}H_2\}\bar{A}lCl_4 + 4CH_4$$

Dimethylphosphine is much less reactive than dimethylamine towards dimethylberyllium and, unlike both dimethylamine and trimethylphosphine, does not appear even to form a co-ordination compound. Heating equimolar quantities to 190° for 5 hours resulted in the formation of about 0·5 mole of methane and non-volatile, evidently polymeric material, insoluble in benzene.

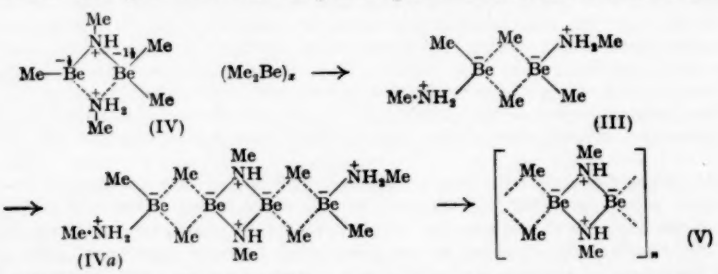
The complex four-stage reaction between dimethylberyllium and methylamine well illustrates the complications due to the presence of two reactive groups instead of one. The initial formation of a 1 : 1 co-ordination compound

$$Me_2Be + NH_2Me \longrightarrow Me_2\bar{B}e{\cdot}\dot{N}H_2Me \text{ (III)}$$

is followed by three successive decompositions at increasing temperatures :

$$2Me_2\bar{B}e{\cdot}\dot{N}H_2Me \longrightarrow (Me_2\bar{B}e{\cdot}\dot{N}H_2Me;\ MeBe{\cdot}NHMe)\ (IV) + CH_4$$
$$(IV) \longrightarrow 2(MeBe{\cdot}NHMe)_x\ (V) + CH_4$$
$$2(V) \longrightarrow (MeBe{\cdot}NHMe;\ Be{:}NMe)_y\ (VI) + CH_4$$

With the exception of the unstable compound (IV) which melts with decomposition at 10°, all these substances are solid and amorphous and are doubtless polymeric. Although (IV) may be a lattice compound between $Me_2\bar{B}e{\cdot}\dot{N}H_2Me$ and MeBe·NHMe, this seems unlikely



(IV) (III) (IV*a*) (V)

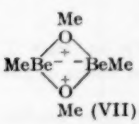
since the latter component is itself likely to be to some degree polymeric (*e.g.*, it was non-volatile at 80°). A fairly simple constitution is indicated by the observation that it melts

relatively sharply, though with decomposition, at a low temperature; the structure (IV) is suggested (broken lines represent half bonds, as in Part II). Another possibility is that the beryllium atoms are bridged by methyl groups (see (IV*a* and V) as in dimethylberyllium itself, the methyl bridge persisting to quite a late stage in the decomposition. However, the simpler alternative, which is similar to the structure given for $(Me_2Be)_2(NMe_3)_3$ in Part II, is preferred.

Since the hydrogen of alcohols is more easily replaced than that of amines it was not surprising to find that dimethylberyllium reacts violently with methanol, even at the melting point of the latter (−98°). The formation of a mixture of liquid and solid during the preparation of methylberyllium methoxide is no doubt due to its further reaction with methyl alcohol, followed, during the heating at 80—90°, by reaction between dimethylberyllium and beryllium dimethoxide:

(*a*) $Me_2Be + Me{\cdot}OH \longrightarrow MeBe{\cdot}OMe + CH_4$
(*b*) $MeBe{\cdot}OMe + MeOH \longrightarrow Be(OMe)_2 + CH_4$
(*c*) $Me_2Be + Be(OMe)_2 \longrightarrow 2MeBe{\cdot}OMe$

A similar observation was made during the preparation of dimethylaluminium methoxide (Brown and Davidson, *loc. cit.*) since trimethylaluminium readily loses all three methyl groups on reaction with alcohols; the reaction between trimethylgallium and methyl alcohol, however, proceeds straight to the final product dimethylgallium methoxide (Coates, unpublished observation) since the remaining methyl groups are relatively unreactive. Methylberyllium methoxide is sufficiently volatile to be distilled in a high vacuum, but on heating, particularly above 120°, disproportionates to a white solid and a colourless liquid, becoming homogeneous again on slow cooling. At temperatures above 120° the vapour pressure of the mixture of solid and liquid is somewhat less than that of dimethylberyllium itself, which is in accordance with a reversal of reaction (*c*). In boiling benzene the substance is dimeric, like dimethylaluminium methoxide and dimethylgallium methoxide, and is similarly assigned a cyclic structure (VII).



(VII)

Although in hydroxylic solvents methanethiol is more acidic than methyl alcohol, the former reacts with dimethylberyllium much less energetically than the latter, methane evolution becoming rapid only at about −10° instead of at −100°. Similarly, Coates (unpublished observations) has observed that trimethylgallium reacts with methanethiol more slowly than with methanol, and with thiophenol more slowly than with phenol.

Anhydrous hydrogen chloride reacts much more slowly with dimethylberyllium than any of the other compounds investigated. Evidence has been given for the view that amines containing reactive hydrogen combine with dimethylberyllium first by the formation of a co-ordination compound. It is not improbable that compounds containing hydroxy- and thiol groups react by a similar mechanism. Now there is no reason why the formation of co-ordination compounds of this type should require an activation energy, unless ligands already present have to be displaced. Consequently the interaction of dimethylberyllium (or, for example, trimethylboron) with donor molecules should be rapid and determined only by the free-energy change. Methyl chloride has been shown by Brown and Davidson (*loc. cit.*) not to react with trimethylaluminium, which is a very strong acceptor, and can thus be considered devoid of donor properties. By the well-known influence of electronegativity of substituents on donor properties, hydrogen chloride must be a still weaker donor; therefore any reaction with dimethylberyllium must involve the breaking of at least one covalent bond, and therefore requires a significant activation energy. As a result the reaction is relatively slow. The product, methylberyllium chloride, is a white solid, less volatile than dimethylberyllium, and evidently highly polymerised. The formation of a layer of relatively non-volatile product covering the dimethylberyllium may also account in part for the low reaction rate.

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THE UNIVERSITY, BRISTOL. [*Received, June 30th*, 1952.]

864. *The Hydrolysis of Amides of Dibasic Acids. Part II.* The Acid Hydrolysis of Oxamide and Oxamic Acid.*

By J. Packer, A. L. Thomson, and J. Vaughan.

Rates of hydrolysis of oxamide and oxamic acid in excess of hydrochloric acid have been measured at 79·5° and at 97·5°. In the conversion of oxamide into oxamic acid, the rate of hydrolysis per amide group is very much less than in the second stage of hydrolysis. No fission of the inter-carbon bond, during hydrolysis, could be detected.

Experimental results reported in Part I * showed that when malonamide is hydrolysed in excess of hydrochloric acid at temperatures between 80° and 100°, the value of the first-order rate constant, k_1 (diamide ⟶ monoamide), is approximately twice that of k_2 (monoamide ⟶ dibasic acid); *i.e.*, the rate of hydrolysis per amide group is approximately the same for both stages of hydrolysis. Under our experimental conditions, therefore, the damping effect of the intervening methylene group is such that the measured rate of hydrolysis of one amide group is not markedly affected by a change, from amide to carboxyl, in the other functional group. In the amides of oxalic acid the functional groups are directly linked and similar kinetic studies should reveal more clearly the expected difference in electronic effects between amide and carboxyl groups. The acid hydrolyses of oxamide and oxamic acid were therefore followed under experimental conditions comparable with those obtaining in the earlier work. In addition, because the inter-carbon bond length in oxamide is high (Misch and van der Wyk, *Arch. Sci. phys. nat.*, 1938, **20**, Suppl. 96), the possibility of hydrolysis being accompanied by fission at this bond was also investigated.

Experimental and Results

Analytical methods and other experimental details were described fully in Part I Hydrolyses were carried out at either 79·5° ± 0·3° or 97·5° ± 0·5°. Dissolution times of the small quantities of solutes used were again too short to affect the kinetics.

Oxamic acid was prepared by Oelkers's method (*Ber.*, 1889, **22**, 1569) and, after several recrystallisations, melted, with decomposition, at 209°.

Oxamic acid reacted extensively with hypobromite but no apparent hydrolysis took place when an aliquot of oxamic acid solution was subjected to the distillation procedure, the buffered solution having a pH of 11·5. This distillation method was therefore used for analysis. A linear $\ln(a - x)$–t plot was obtained in each hydrolysis run (Fig. 1), and the rate constant obtained therefrom was unaltered by variation in the amide : acid ratio, thus confirming the pseudounimolecular nature of the reaction. Hydrolyses were followed within the range [HCl] = 0·0156—0·75M, and the mean values for k_2 at any given concentration of hydrochloric acid were plotted against the molar concentration of acid, giving a linear plot at each temperature (Table). The graphs can be defined by the equations

$$k_2 = 0{\cdot}0008 + 0{\cdot}0475\ [\mathrm{HCl}]\ (\text{at } 79{\cdot}5°);\quad k_2 = 0{\cdot}007 + 0{\cdot}184\ [\mathrm{HCl}]\ (\text{at } 97{\cdot}5°)$$

and the approximate activation energy, from these results, is 20·5 kcal. mole^{-1}.

Oxamide was prepared by ammonolysis of ethyl oxalate and, before use, was repeatedly recrystallised from water.

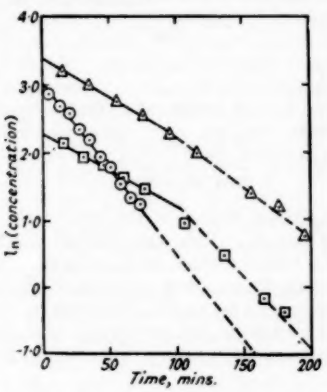
Estimation of ammonia in the presence of oxamide was not easy. The direct titration method was at first disregarded because hypobromite reacted with oxamide. The distillation method, as employed successfully for oxamic acid, was useless because oxamide was hydrolysed to a considerable extent in the relatively strongly alkaline solution; this fact is in accord with the results of Westheimer and Shookoff (*J. Amer. Chem. Soc.*, 1940, **62**, 269) who have shown that oxamide is hydrolysed, in alkaline solution, about 100 times faster than oxamic acid. By reducing the pH of the buffered solution to 9·8, however, it was possible to effect 100% recovery of ammonia in 15 minutes, with only 3·5% hydrolysis of the amide. This error, although not insignificant, was by no means large, and allowance could be made for it. A series of hydrolyses were therefore followed at each of the two temperatures. In all cases the $\ln(a - x)$–t plots were reproducible up to about 50% hydrolysis, consistent values being obtained for $k(= k_1/2$; see

* Part I, *J.*, 1952, 3264.

Part I). In each instance the logarithmic plot deviated from linearity after the hydrolysis had reached a half-way stage, but consistency was thereafter absent. On occasions the graph broke sharply at this point to give a new straight line from which could be obtained a rate constant somewhat similar to that obtained for oxamic acid hydrolysis (k_2); at other times the deviation from the initial slope was only slight (Fig. 1). The majority of results fell between the two extremes. The inconsistent results obtained for this stage of the hydrolysis are presumably due to the limitations of the analytical method employed. Although relative possible errors will increase with time owing to the decrease in value of the $(a - x)$ term and thus of the titre, the very much lower pH of the distillation buffer (as compared with that used for oxamic acid) further reduces accuracy. With oxamide this analytical method is clearly reaching the limits of application and fails to give reliable information concerning the second stage of oxamide hydrolysis. However, the k_1 values may be combined with values for k_2, obtained from work on oxamic acid itself, to give a picture of oxamide hydrolysis. Rate constants $k(= k_1/2)$ were again determined at several acid concentrations, at the two specified

FIG. 1.

Hydrolyses in 0·50M-hydrochloric acid at 79·5°.

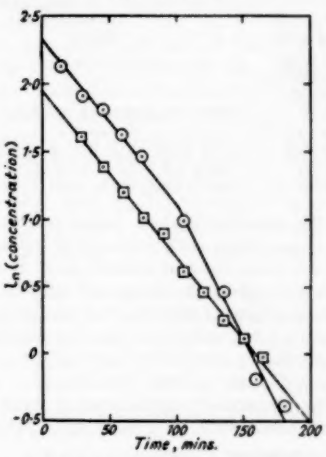


Analysis by distillation method.

○ Oxamic acid.
□ Oxamide.
△ Oxamide, graph displaced by one ordinate unit.

FIG. 2.

Hydrolysis of oxamide in 0·50M-hydrochloric acid at 79·5°.



⊙ Analysis by distillation method.
⊡ Analysis by direct titration method.

temperatures. The plot of k against [HCl] at each temperature is a linear one (Table) which passes through the origin and may be described by one of the simple equations:

$$k = 0{\cdot}0249\ [\mathrm{HCl}]\ (\text{at } 79{\cdot}5°);\quad k = 0{\cdot}0972\ [\mathrm{HCl}]\ (\text{at } 97{\cdot}5°)$$

The approximate energy of activation is 20·5 kcal. mole^{-1}.

The direct titration method, as applied to oxamide, is worthy of further mention because a more detailed examination led to a curious kinetic result. In the reaction between hypobromite and oxamide one mole of hypobromite was found to be consumed per mole of oxamide. The reaction took 3 minutes for completion under our experimental conditions and no further consumption of hypobromite was noted even after some considerable time. This reaction corresponds to an apparent 33% hydrolysis of oxamide. Hydrolysis runs were carried out on oxamide, the direct titration method being used, and the natural logarithm of "apparent concentration of oxamide" was plotted against time. The resulting graph was in each case linear and of slope identical with that of the linear portion of the graph obtained by use of the distillation method. The plot could, however, be projected back to a point on the logarithm axis corresponding to 33% hydrolysis of the oxamide (Fig. 2). This is explicable only in part, and the explanation is only valid for the time during which the oxamic acid intermediate is not present in high concentration. If the extent of the hypobromite–oxamide reaction were constant for all hydrolysate samples during a given experiment, this reaction would show up in each titre as an apparent increase in the extent of hydrolysis; the increase would be

proportional (33%) to the amount of unhydrolysed oxamide. It may readily be shown that the graph of " ln(apparent concentration of oxamide)–time " should have the same slope as that of " ln(actual concentration)–time " and should be displaced to the same extent as that found experimentally. This simple explanation can apply, however, only while the concentration of oxamic acid, which itself reacts with hypobromite, is low. It is true that the early stages of the hydrolysis should be almost free from this complication but calculation of oxamic acid concentrations [by Swain's method (*J. Amer. Chem. Soc.*, 1944, **66**, 1691)] indicates that at 20% hydrolysis the oxamic acid concentration becomes sufficiently large to invalidate the above conclusion. The fact remains, however, that in every case the monolinear form is maintained for the whole of the hydrolysis, and the logarithmic plots lead to rate constants duplicating those obtained for k by the distillation method. Thus the direct titration method could, in practice, be used to extend the number of k values obtained by the more laborious, alternative procedure, and has in fact been so used. The nature of the reaction between oxamide and hypobromite is also not clear, although from the definite reaction proportions, and from Foster's work (*J.*, 1878, **33**, 470; 1879, **35**, 119) it appears possible that initially monobromination occurs. There

10^3 *Rate constants* (*min.*$^{-1}$)

Molarity of acid	Oxamide ($k = k_1/2$)		Oxamic acid (k_2)	
	79·5°	97·5°	79·5°	97·5°
0·0156	—	[1·1]	—	17·8, 17·8
0·0625	—	6·2, 6·7	—	—
0·125	—	13·0, 13·0	—	30·4, 30·6
0·25	6·05, 6·15, 6·18, 6·02, 6·12	23·4, 24·1	12·9, 12·9, 12·6, 13·0	54·0, 53·0
0·35	—	33·8, 33·6	—	70·0, 70·0
0·375	8·3, 10·5, 10·2, 8·8, 9·8, 9·2	—	17·5, 18·0, 18·3	—
0·50	11·5, 12·7, 12·2, 11·9, 12·9, 12·9	48·3, 49·3	25·0, 25·0, 25·5	96, 99
0·75	18·4, 18·4, 18·6, 19·0, 19·2, 18·9	—	39·4, 33·0, 36·0	—

was the possibility that, under our experimental conditions, fission of the inter-carbon bond may take place, with consequent release of oxides of carbon. This was checked during runs on both oxamide and oxamic acid at the lower of the two reference temperatures. Dry air, free from carbon monoxide and carbon dioxide, was drawn through the contents of the reaction vessel throughout the run, the emergent gases being examined for oxides of carbon by standard methods. No positive tests were obtained although the reagents had previously been shown to be sufficiently sensitive to reveal the presence of carbon oxides resulting from any appreciable amount of inter-carbon bond fission.

The theoretical significance of these results is being reserved for discussion in a later paper, when related work on a number of substituted malonamides has been completed.

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NOTES.

865. *Some Complex Organic Salts of Stannous Tin.*

By E. H. BAKER and F. C. TOMPKINS.

THE tendency for stannous tin to form complex salts is marked: a series of complex formates having the general formula $M_2Sn(H{\cdot}CO_2)_4,5H_2O$, where M = Na, NH_4, or K, were prepared by Elöd and Kolbach (*Z. anorg. Chem.*, 1927, **164**, 297), and a stannous oxyacetate was isolated by Glassman (*Ber.*, 1908, **41**, 36) who showed its constitution to be $Sn_2O(CH_3{\cdot}CO_2)_2$, later confirmed by Elöd and Kolbach (*loc. cit.*). Preparations of complex acetates, however, have not been reported.

During a study of the autoxidation rates of stannous acetate in solution, it was found necessary to investigate the possibility of complex-salt formation in alkali acetate–stannous acetate solutions, and two complex acetates, stannous ammonium acetate and stannous calcium acetate, were isolated.

EXPERIMENTAL

Stannous Ammonium Acetate.—Stannous chloride dihydrate ("AnalaR"; 42 g.) was dissolved in distilled water (200 ml.), and ammonia solution (d 0·880) added with stirring until the mixture

was alkaline to phenolphthalein. The stannous hydroxide was filtered off and washed with hot distilled water until free from chloride. It was then refluxed under nitrogen with glacial acetic acid (60 ml.) containing ammonium acetate (14 g.), until completely dissolved. Distillation of the solution was continued until a thick syrup (40 ml.) remained. Benzene (150 ml.) and absolute alcohol (150 ml.) were added, and distillation under nitrogen continued in order to remove most of the residual water. When the volume had been reduced to 150 ml., the flask was cooled at 0° for 1—2 days, whereupon the complex crystallized out. The crystals were filtered off under nitrogen, washed with benzene–alcohol (45—50%) containing glacial acetic acid (5%), and recrystallized from the same solvent. The final product, after being washed with alcohol, then light petroleum (b. p. 40—60°), and dried in a desiccator, was obtained in about 50% yield as colourless prisms, m. p. 138° [Found: C, 25·5; H, 4·4; N, 4·3; Sn, 34·9, 35·0. $NH_4Sn(CH_3{\cdot}CO_2)_3,\frac{1}{2}C_6H_6$ requires C, 25·7; H, 4·3; N, 4·3; Sn, 36·3%].

This *complex* is non-hygroscopic but freely soluble in water with hydrolysis to give a cloudy solution. Clear solutions are obtained in dilute acetic acid or acetic acid–ammonium acetate solution. On dissolution in water, a small quantity of benzene retained from the preparation (see analysis) was released; the benzene was so firmly held that even after a year at room temperature and drying at 60°/10 mm. for 3 hours, an identical analysis was obtained. This firm retention of benzene and its release in aqueous solution suggest the possibility of a clathrate type of compound. The complex is insoluble in benzene itself.

Stannous Calcium Acetate.—Calcium acetate (1·7 g.) was dissolved in hot distilled water (15 ml.) at 80°; glacial acetic acid (2 ml.) and stannous acetate solution (10 ml., 1·5M) were added with stirring. The calcium complex, which quickly crystallized from the warm solution, was filtered off under nitrogen. After being washed with alcohol containing a little acetic acid, then light petroleum (b. p. 40—60°), and dried in a desiccator, the product formed colourless, non-hygroscopic leaflets (yield, 70%). It had no definite m. p., but decomposed slowly at about 260° [Found: C, 23·45; H. 3·2; Ca, 6·3; Sn, 37·3. $CaSn_2(CH_3{\cdot}CO_2)_6$ requires C, 22·8; H, 2·85; Ca, 6·35; Sn, 37·6%]. This *complex* was less soluble in water than the ammonium analogue but again hydrolysed giving a cloudy solution. Clear solutions could be obtained in water strongly acidified with acetic acid or in dilute acetic acid containing an excess of calcium acetate.

Stannous Ammonium Chloroacetate.—This *compound* was prepared in a similar way: stannous hydroxide (*ex* "AnalaR" $SnCl_2,2H_2O$, 37 g.) was refluxed with 150 ml. of chloroacetic acid (42 g.) to which ammonia (*d* 0·880; 8 ml.) had been added; large colourless prisms, m. p. 187° (decomp.), were obtained on crystallization (yield, *ca.* 80%) [Found: C, 17·5; H, 2·5; N, 3·1; Cl, 25·1; Sn, 28·0. $NH_4Sn(CH_2Cl{\cdot}CO_2)_3$ requires C, 17·3; H, 2·4; N, 3·4; Cl, 25·5; Sn, 28·4%]. In cold water containing sufficient free acid to prevent hydrolysis, this compound was only slightly soluble, thus differing from the analogous acetate.

One of us (E. H. B.) thanks the Tin Research Institute for the award of a grant held during this work.

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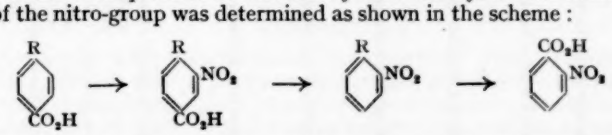
866. *The Preparation of Some* 4-n-*Alkyl*-3-*nitrobenzoic Acids.*

By Hussein A. Fahim and Abdallah M. Fleifel.

The *p*-alkylbenzoic acids used as starting material were prepared by alkaline fusion of the corresponding *p*-alkylphenyl methyl ketones at temperatures between 200° and 280°. They were best nitrated by fuming nitric acid alone or by a mixture of concentrated nitric and sulphuric acids. The product was invariably the 4-*n*-alkyl-3-nitrobenzoic acid in which the position of the nitro-group was determined as shown in the scheme:



Experimental.—*Nitration.* (i) The aromatic acid was added gradually to stirred nitric acid (*d* 1·5) at 0°, the mixture being kept at this temperature for 1 hour more, then overnight at room

Compound	M. p. or b. p./mm.	Crystn. solvent *	Found, %: C	H	N	Formula	Required, %: C	H	N
(a) *4-Alkyl-3-nitrobenzoic acids and derivatives.*									
4-Ethyl-3-nitrobenzoic acid	153—154° †	A	55·4	4·6	7·3	$C_9H_9O_4N$	55·4	4·6	7·2
,, acid chloride	242—244°/760	—	—	—	—	—	—	—	—
,, amide	110—111	A	55·3	5·2	14·7	$C_9H_{10}O_3N$	55·7	5·1	14·4
,, methylamide	94—95	,,	57·5	5·8	13·4	$C_{10}H_{12}O_3N_2$	57·7	5·8	13·4
3-Nitro-4-*n*-propylbenzoyl chloride	171—172/8	—	—	—	—	—	—	—	—
,, amide	119—120	A	57·8	5·6	13·2	$C_{10}H_{12}O_3N_2$	57·7	5·8	13·4
,, methylamide	68—69	,,	59·4	6·4	12·4	$C_{11}H_{14}O_3N_2$	59·4	6·3	12·6
4-*n*-Butyl-3-nitrobenzoic acid	138—139	B	59·1	5·6	6·4	$C_{11}H_{13}O_4N$	59·2	5·8	6·3
,, acid chloride	180/7	—	—	—	—	—	—	—	—
,, amide	115—116	A	59·8	6·2	12·5	$C_{11}H_{14}O_3N_2$	59·4	6·3	12·6
,, methyl amide	96—97	,,	60·7	6·7	12·1	$C_{12}H_{16}O_3N_2$	61·0	6·8	11·9
4-*n*-Amyl-3-nitrobenzoic acid	127—128	B	60·7	6·2	5·8	$C_{12}H_{15}O_4N$	60·7	6·3	5·9
,, acid chloride	192—193/20	—	—	—	—	—	—	—	—
,, amide	113—114	A	61·1	6·7	11·9	$C_{12}H_{16}O_3N_2$	61·0	6·8	11·9
,, methyl amide	67—68	,,	62·5	7·3	10·9	$C_{13}H_{18}O_3N_2$	62·4	7·2	11·2
4-*n*-Hexyl-3-nitrobenzoic acid	113—114	B	62·2	6·7	5·6	$C_{13}H_{17}O_4N$	62·1	6·8	5·6
,, acid chloride	187—188/23	—	—	—	—	—	—	—	—
,, amide	94·5—95·5	A	62·1	7·0	11·0	$C_{13}H_{18}O_3N_2$	62·4	7·2	11·2
,, methyl amide	56—57	C	63·1	7·7	10·8	$C_{14}H_{20}O_3N_2$	63·6	7·6	10·6
4-*n*-Heptyl-3-nitrobenzoic acid	89—90	,,	63·6	7·3	5·2	$C_{14}H_{19}O_4N$	63·4	7·2	5·3
,, acid chloride	193—194/12	—	—	—	—	—	—	—	—
,, amide	87—88	A	63·2	7·8	10·4	$C_{14}H_{20}O_3N_2$	63·6	7·6	10·6
,, methyl amide	54—55	B	65·1	7·7	9·9	$C_{15}H_{22}O_3N_2$	64·7	7·9	10·1
3-Nitro-4-*n*-octylbenzoyl chloride	204—205/10	—	—	—	—	—	—	—	—
,, amide	68—69	A	65·2	8·0	10·3	$C_{15}H_{22}O_3N_2$	64·7	7·9	10·1
,, methyl amide	52—53	B	66·4	8·5	9·8	$C_{16}H_{24}O_3N_2$	65·7	8·2	9·6
(b) *Derivatives of* 4-n-*alkylbenzoic acids.*									
4-*n*-Amylbenzoyl chloride	144—145/10	—	—	—	—	—	—	—	—
,, amide	147—148	C	75·5	8·9	7·0	$C_{12}H_{17}ON$	75·4	8·9	7·3
,, methyl amide	91—92	A	76·0	9·1	6·9	$C_{13}H_{19}ON$	76·1	9·3	6·8
4-*n*-Hexylbenzoyl chloride	176—177/22	—	—	—	—	—	—	—	—
,, amide	141—142	A	76·2	9·4	6·5	$C_{13}H_{19}ON$	76·1	9·3	6·8
,, methyl amide	80—81	C	76·4	9·7	6·1	$C_{14}H_{21}ON$	76·7	9·6	6·4
4-*n*-Heptylbenzoyl chloride	195—196/40	—	—	—	—	—	—	—	—
,, amide	147—148	A	76·5	9·7	6·1	$C_{14}H_{21}ON$	76·7	9·6	6·4
,, methyl amide	95—96	,,	77·4	9·8	6·1	$C_{15}H_{23}ON$	77·3	9·9	6·0
4-*n*-Octylbenzoyl chloride	188/12	—	—	—	—	—	—	—	—
,, amide	139—140	D	77·8	10·1	6·1	$C_{15}H_{23}ON$	77·3	9·9	6·0
,, methyl amide	84—85	A	77·8	10·2	5·6	$C_{16}H_{25}ON$	77·7	10·1	5·7

* A = benzene–light petroleum; B = light petroleum; C = aqueous ethanol; D = benzene.

† Aschenbrandt, *Annalen*, 1883, **216**, 211, gave m. p. 155—156°.

temperature; the nitro-acid was then precipitated by addition of ice-cold water. (ii) The aromatic acid was added gradually to nitric acid (*d* 1·4) and concentrated sulphuric acid at 5—10°, and the reaction mixture treated as in (i). The 4-alkyl-3-nitrobenzoic acids and some of their derivatives are listed in the Table (section *a*) (p. 4520), and derivatives of 4-*n*-alkylbenzoic acids in section *b*.

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867. *The Synthesis of βγ-Unsaturated α-Keto-acids from 1 : 1-Diarylethylenes.*

By FELIX BERGMANN and ABRAHAM KALMUS.

IN Friedel–Crafts reactions of aromatic hydrocarbons with oxalyl chloride the diaryl ketone is the usual product, but 1 : 2-diketones may also be formed (Staudinger, *Ber.*, 1912, **45**, 1596). However, the isolation of an α-keto-acid has not hitherto been reported. Kharasch, Kane, and Brown (*J. Amer. Chem. Soc.*, 1942, **64**, 333) found that the uncatalyzed reaction of 1 : 1-diarylethylenes with oxalyl chloride leads to ββ-diphenylacrylyl chloride (I) with elimination of carbon monoxide and hydrogen chloride. When we followed quantitatively the analogous reaction with 1 : 1-di-*p*-chlorophenylethylene (F. Bergmann *et al.*, *ibid.*, 1948, **70**, 1612), we observed that evolution of carbon monoxide lags considerably behind that of hydrogen chloride. The syrupy reaction mixture was found to contain a small amount of a second acid, m. p. 135—136°. Analysis indicated formula (II; R = H), and the acid was slowly decomposed by boiling oxalyl chloride to ββ-di-*p*-chlorophenylacrylic acid (III).

Independent evidence for the structure of the α-keto-acid (II; R = H) was obtained by condensation of di-*p*-chlorophenylethylene with ethoxalyl chloride at 180°, which gave the ester (II; R = Et) in about 10% yield. The acid obtained by hydrolysis of this ester was identical with the acid, m. p. 135—136°. The keto-ester was characterized by its 2 : 4-dinitrophenylhydrazone and its ultra-violet absorption spectrum (see Table).

Absorption spectra of ethyl esters of type (II).

Ethyl ester	Minimum λ, Å	Minimum log $\epsilon_{mol.}$	Maximum λ, Å	Maximum log $\epsilon_{mol.}$	Minimum λ, Å	Minimum log $\epsilon_{mol.}$	Maximum λ, Å	Maximum log $\epsilon_{mol.}$
2-Keto-4 : 4-diphenylbut-3-enoate	2200	4·00	2300	4·02	2570	3·60	3140	4·12
4 : 4-Di-*p*-chlorophenyl-2-ketobut-3-enoate	2200	4·13	2320	4·21	2600	3·78	3170	4·18

The reaction proved to be general, and the corresponding keto-ester (and acid) was prepared from 1 : 1-diphenylethylene. Its absorption spectrum resembles very closely that of the dichloro-ester (see Table).

The synthesis and properties of this new class of βγ-unsaturated α-keto-acids are being studied further.

$$CPh_2{:}CH_2 + (COCl)_2 \longrightarrow CPh_2{:}CH{\cdot}COCl\ (I) + CO + HCl$$

$$(p\text{-}Cl{\cdot}C_6H_4)_2C{:}CH_2 + (COCl)_2 \begin{cases} \nearrow (p\text{-}Cl{\cdot}C_6H_4)_2C{:}CH{\cdot}CO{\cdot}CO_2R\ (II) \longleftarrow (p\text{-}Cl{\cdot}C_6H_4)_2{:}CH_2 + COCl{\cdot}CO_2R \\ \searrow (p\text{-}Cl{\cdot}C_6H_4)_2C{:}CH{\cdot}CO_2H\ (III) \end{cases}$$

EXPERIMENTAL

Ethoxalyl chloride (Diels and Nawiasky, *Ber.*, 1904, **37**, 3678; Fourneau and Sabetay, *Bull. Soc. chim.*, 1927, **41**, 537) is conveniently prepared as follows: Ethyl hydrogen oxalate (1 mol.) and thionyl chloride (1·5 mol.) were heated under reflux in an oil-bath at 135°, while dry nitrogen was bubbled through. After 6 hours the mixture was fractionated, and the ester chloride obtained in 90—95% yield, having b. p. 39—40°/18 mm.

Condensation with 1 : 1-*Di*-p-*chlorophenylethylene*.—The ethylene (8·3 g.) and ethoxalyl

chloride (9 g., 2 equiv.) were heated to 180° in an oil-bath and kept at 180—190° for 2 hours while dry nitrogen was bubbled through. The brown mass was dissolved in benzene and washed with saturated sodium hydrogen carbonate. Fractionation *in vacuo* gave an oil, b. p. 195—200°/1 mm., which gradually crystallized. From propanol, 1 g. of *ethyl* 4 : 4-*di*-p-*chlorophenyl*-2-*ketobut*-3-*enoate* was obtained in long prismatic columns, m. p. 93—94° (Found : C, 62·2; H, 4·0. $C_{18}H_{14}O_3Cl_2$ requires C, 61·9; H, 4·0%). Hydrolysis at room temperature with 2·5% ethanolic potassium hydroxide and working up as usual gave the free *acid*, and several recrystallizations from benzene–light petroleum gave prismatic rods, m. p. 134—135° (Found : C, 59·8; H, 3·3. $C_{16}H_{10}O_3Cl_2$ requires C, 59·8; H, 3·1%). The ester yielded a 2 : 4-*dinitrophenylhydrazone*, which crystallized from butanol in hexagonal plates, m. p. 202—205° (Found : N, 10·3. $C_{24}H_{18}O_6N_4Cl_2$ requires N, 10·6%).

Condensation with 1 : 1-*Diphenylethylene*.—The ethylene (10 g.) and ethoxalyl chloride (15 g.) were heated for 6 hours in an oil-bath at 180—190°. Treatment as above gave a yellow oil, b. p. 177—178°/1 mm., which solidified spontaneoulsy after two redistillations. From light petroleum, 3 g. of *ethyl* 2-*keto*-4 : 4-*diphenylbut*-3-*enoate* were obtained as prisms, m. p. 49—50° (Found : C, 76·9; H, 5·7. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%). The 2 : 4-*dinitrophenylhydrazone* crystallized from butanol in branched prismatic rods, m. p. 180—184° (Found : N, 11·9. $C_{24}H_{20}O_6N_4$ requires N, 12·2%). The corresponding *acid* was obtained as an oil and was purified as follows : it was dissolved in ethanol and an equal volume of water added, whereupon the solution became turbid; when this mixture was heated, most of the turbidity disappeared, and a dark oil separated; after addition of charcoal the mixture was boiled for 1 minute and filtered; the rods, which crystallized upon cooling, were purified from ligroin, forming long needles, m. p. 125° (Found : C, 76·5; H, 5·2. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%).

Isolation of 4 : 4-*Di*-p-*chlorophenyl*-2-*ketobut*-3-*enoic Acid from the Reaction with Oxalyl Chloride*.—The ethylene (8 g.) and oxalyl chloride (15 g.) were kept at 30° for 1 week. The excess of chloride was removed *in vacuo*, and the residue mixed with excess of 10% sodium hydroxide solution. After 6 hours at room temperature the mixture was boiled with charcoal and filtered hot. The sodium salts, which crystallized on cooling, were removed and added to ice-cold hydrochloric acid. The crude acid (10 g.) melted at about 70°. It was dissolved in dilute acetic acid and left in a Dewar flask for over a month. The crystals were of two forms—long needles and clumps. The rather small amount of needles was separated mechanically and recrystallized first from dilute methanol (needles), then twice from benzene–light petroleum, forming prismatic rods, m. p. 135—136° undepressed on admixture with the acid (II; R = H) above. The clumps were recrystallized from dilute acetic acid, then from benzene–light petroleum; this compound, m. p. 175°, is identical with ββ-di-*p*-chlorophenylacrylic acid (cf. F. Bergmann *et al.*, *loc. cit.*).

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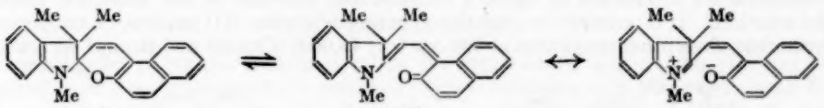
868. *Formation of Coloured Forms of Spirans by Low-temperature Irradiation.*

By Ernst Fischer and Yehuda Hirshberg.

It has been reported (Hirshberg, *Compt. rend.*, 1950, **72**, 5009) that certain derivatives of dianthronyl are reversibly converted into coloured modifications by irradiation at low temperatures. Similar observations with certain spirans are now reported. Several spirans exist in solution in thermal equilibrium with coloured modifications, the concentration of the latter increasing with temperature (see Koelsch, *J. Org. Chem.*, 1951, **16**, 1362, and Knott, *J.*, 1951, 3038, where previous literature is listed). Chaudé and Rumpf (*Compt. rend.*, 1951, **233**, 405) found from the plots of the logarithm of the molar extinction coefficients against the reciprocal of the absolute temperature, for a series of such compounds, that the heats of conversion into the coloured modification were 2—6 kcal./mole. By assuming that at infinite temperature this conversion is virtually complete, they estimated the molar extinction coefficient of the pure coloured form by extrapolation to $1/T = 0$.

The coloured modifications are generally believed to be resonance hybrids of quinoid and bipolar forms (Koelsch, *loc. cit.*; Knott, *loc. cit.*). Thus, for 1 : 3 : 3-trimethylindoline-

2-*spiro*-6′-(2′ : 3′-β-naphthopyran) (I), solutions of which become pink when heated, equilibrium with a hybrid of (I*b*) and (I*c*) has been postulated (Bergmann, Weizmann, and Fischer, *J. Amer. Chem. Soc.*, 1950, **72**, 5009).



When solutions of (I) are irradiated for about a minute at below −50°, they become intense violet-red. No such effect is observed with the solid compound, but in supercooled solutions in ethanol–methanol coloration occurs to some extent even at liquid-air

FIG. 1. *Absorption spectra for spiran* (I) : (*a*) *at low temperature*; (*b*) *at* 25°; (*c*) *at* 135°.

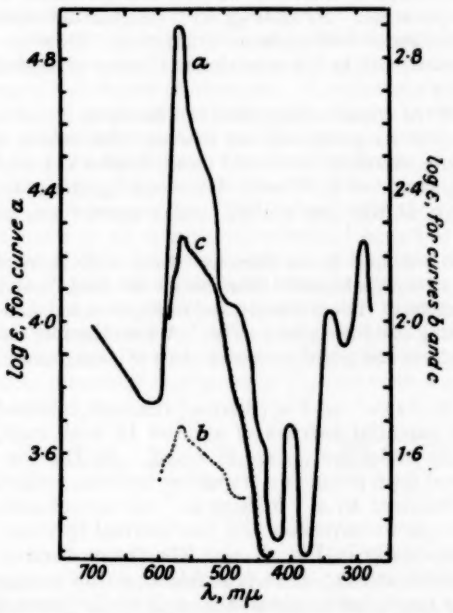
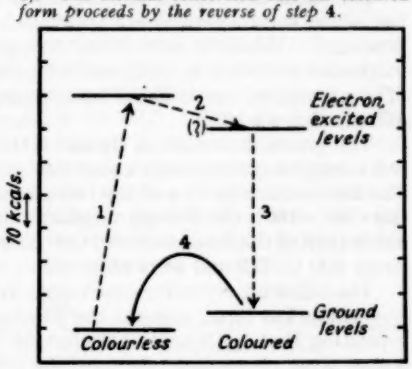


FIG. 2. *Schematic representation of photoconversion* (*steps* 1, 2, 3) *and thermal reversion* (*step* 4). *The thermal conversion into the coloured form proceeds by the reverse of step* 4.



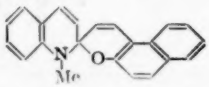
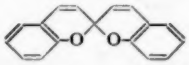
temperature. Fig. 1, curve *a*, represents the absorption spectrum at −100° of a solution irradiated at this temperature to maximum absorption intensity. Curves *b* and *c* give the absorption spectra of solutions at 25° and 135°. The similarity between the temperature-dependent absorption band in *b* and *c* and the corresponding band in *a* is evident.

The molar extinction coefficient of the irradiated solution at the maximum (about 570 mμ) is approximately 88,000, in good agreement with the value of 100,000 estimated by Chaudé and Rumpf (*loc. cit.*) for the coloured species. It therefore appears plausible that the coloured modifications formed by either heat or low-temperature irradiation are identical, and that in the latter process practically complete conversion into the coloured form takes place.

On storage, the irradiated solution loses its colour at a rate dependent on temperature, and the cycle is indefinitely reversible. The rate of this reverse reaction was measured at several temperatures between −30° and −50°. By assuming the reaction to be of the first order, its critical increment was estimated graphically [the plot of log (reversion time) against $1/T$ was linear]; the resulting value, 15 ± 2 kcal./mole, may be regarded as a minimum for the potential barrier between the coloured and the colourless form; the

actual activation energy for such a complex molecule may be considerably higher. The frequency factor calculated from the above observations is about $10^{12\cdot5}$.

If the coloured form is a resonance hybrid of (I*b*) and (I*c*), one would expect the low-temperature irradiation to cause a considerable increase in the dielectric constant of the solution. It is noteworthy that the structurally similar (II) possesses a temperature-independent absorption maximum at 600 mμ ($\varepsilon = 45{,}000$) (Chaudé and Rumpf, *loc. cit.*) and

(II)   (III)

a dipole moment of about 10 D (Bergmann *et al.*, *loc. cit.*). The latter authors have therefore suggested that conversion of this compound into a hybrid, analogous to (I*b*) ⟷ (I*c*), is complete even at room temperature.

The dielectric constants of heptane and toluene solutions of (I) were measured at −78°, before and after irradiation at this temperature. By analogy with (II), the dielectric constant of these solutions should increase by about 0·09 units on irradiation. However, no increase in dielectric constant was observed, within the experimental error of 0·0005 unit.*

No colour develops on heating solutions of the colourless spiran (III) (Koelsch, *loc. cit.*), but when such solutions are irradiated at low temperatures, an intense blue colour is produced. From the rates of the disappearance of colour at several temperatures a critical increment of 17·5 kcal./mole and a frequency factor of $10^{14\cdot5}$ were determined graphically. [The absorption curve has a broad maximum at 670 (log ε 4·39), and a narrow one at 470 mμ (log ε 4·16).]

The photoconversion of (I) and (III) into coloured forms does not occur with light of wave-lengths greater than about 540 mμ (*i.e.* energies lower than about 65 kcal./mole). The fluorescence spectra of the two modifications of (I) were measured in supercooled solutions at −180°, the 365-mμ mercury line being used as light source. A considerable enhancement of the fluorescence of the coloured form and a bathochromic shift of its maximum (from 600 to 615 mμ) were observed.

The following tentative conclusions may be drawn : (*a*) The (thermal) reaction, coloured ⟶ colourless form, requires the passing of potential barriers of at least 15 kcal./mole, indicating that configurational changes in the molecules (I) are involved. (*b*) The low-temperature photoconversion into the coloured form involves a transition between excited electronic states of the two modifications, followed by a " freezing-in " of the coloured form. The postulated steps involved in the photoconversion and the thermal reversion over a potential barrier are presented schematically in Fig. 2. (*c*) Non-thermochromic spirans [*e.g.* (III)] also exist in coloured modifications; it is probable that the energy difference between the two modifications is so large that no observable shift of the thermal equilibrium towards the coloured form can occur within the accessible temperature range. This increased energy difference does not affect the photoconversion which proceeds by a different mechanism, and is independent of the thermal equilibrium. (*d*) Bipolar mesomers do not contribute materially to the structure of the coloured modifications described.

We are grateful to Dr. Anna Weizmann for samples of compounds (I) and (III).

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* In a previous communication (Bergmann *et al.*, *loc. cit.*) it was reported that the dipole moment of (I) at 90° is not significantly larger than that at 30°. However, these results were inconclusive, since at this temperature only a small percentage of the substance exists in the coloured modification.

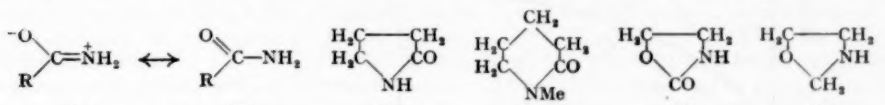
869. *Electric Moments and Intermolecular Hydrogen Bonds of Cyclic Amides and Oxazolidones.*

By Ernst Fischer.

The contribution of bipolar mesomers (I) to the structure of acid amides (II) has been estimated from a comparison of the observed electric moments with those calculated from bond moments or from the moments of simpler molecules (see Bates and Hobbs, *J. Amer. Chem. Soc.*, 1951, **73**, 2151, where previous literature is listed).

Because of the non-planarity of the nitrogen valencies, and the possible rotation about the carbon–nitrogen bond in (II), calculations of the moment of (II) from bond moments must be based on some assumption with regard to the configuration of (II) in solution. Such assumptions are generally not unambiguous, and as a result some controversy has recently arisen with regard to the significance of the conclusions reached (Kumler, *ibid.*, 1952, **74**, 261).

The configuration of cyclic amides, such as pyrrolid-2-one (III), is free from these ambiguities, and their moments can therefore be estimated from bond moments with a reasonable degree of accuracy. Comparison with the experimental moments may then lead to more conclusive results with regard to the contribution of bipolar mesomers. The experimental moments of 2·9 D for *cyclo*pentanone (Gunthard and Gaumann, *Helv. Chim. Acta*, 1951, **34**, 39) and 1·6 D for pyrrolidine (Robles, *Rec. Trav. chim.*, 1939, **58**, 111) permit calculation of the moment for the planar model of (III) as about 3·9 D, the value assumed for the angle between the N–H valency and the ring plane scarcely affecting this figure. Unfortunately no reliable experimental figures are available for (III). For 1-methylpiperid-2-one (IV) in benzene solution a moment of 4·0 D was found (Syrkin and Shott-Levova, *Acta Physicochim. U.R.S.S.*, 1945, **20**, 397) which would correspond to a value of about 4·2 D for the non-methylated piperid-2-one. Since the relative position of the polar bonds in this molecule will not differ much from that in (III), this figure may be compared with the "theoretical" value of 3·9 D. If the difference (0·3 D) is ascribed to the contribution of bipolar mesomers analogous to (I), this contribution would amount to about 5%.



(I) (II) (III) (IV) (V) (VI)

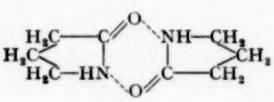
Analogously, the moment of the planar, pentagonal model of oxazolid-2-one (V) would be about 4·1 D, based on the experimental moments of 1·6 D for oxazolidine (VI) (Bergmann, Fischer, Zimkin, and Pinchas, *Rec. Trav. chim.*, 1952, **71**, 213) and 2·9 D for *cyclo*pentanone. For 1-methyloxazolid-2-one in benzene solution a moment of 5·04 ± 0·05 D was found; the same value was observed for extremely dilute solutions (see below) of oxazolid-2-one itself. From the difference of about 1 D between the calculated and the observed moment, a contribution of about 16% from bipolar mesomers analogous to (I) is calculated for (V).

Amides tend to associate in benzene solutions, the predominant product in dilute solutions ($\chi < 0{\cdot}005$) being the ring dimer (VII), in which the two molecules are held together mainly by two hydrogen bonds.* Hobbs and Bates (*J. Amer. Chem. Soc.*, 1952, **74**, 746) have recently estimated the corresponding dimerisation constants from the deviations from linearity of the curves of dielectric constant increment ($\Delta\varepsilon$) *versus* concentration.

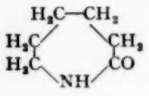
The present measurements show that for oxazolidone this association is very much more pronounced. In the Figure values of $\Delta\varepsilon$ of benzene solutions are recorded at weight fractions up to about 0·008, for oxazolidone (V), 1-methyloxazolid-2-one and 6-amino-

* Mizushima, Simanouti, Nagakura, Kuratani Tsuboi, Baba, and Fujioka (*J. Amer. Chem. Soc.*, 1950, **72**, 3490) found that in carbon tetrachloride solutions of *N*-methylacetamide, unlike those of the amides of types (II) and (III), association takes place to give chains rather than rings.

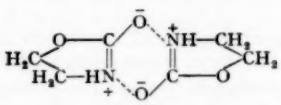
hexanoic lactam (VIII), the latter serving as a representative cyclic amide. It is evident from a comparison of the three curves (*a*) that the deviation from linearity of the curve is much larger for (V) than for (VIII) and (*b*) that no such deviation occurs when the *N*-hydrogen atom is replaced by methyl. It follows from these observations that association



(VII)



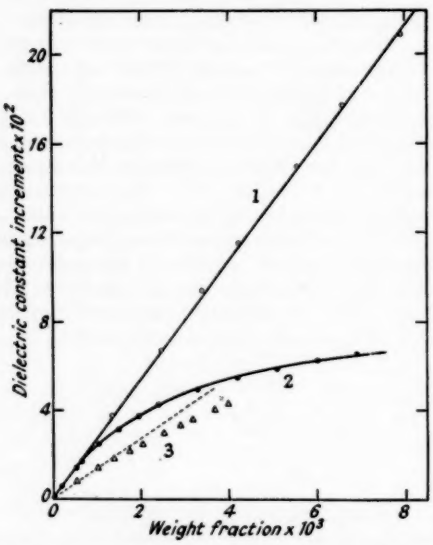
(VIII)



(IX)

in this range of concentration is due mainly to the formation of intermolecular hydrogen bonds and that this type of association is much more pronounced in solutions of oxazolidone than in cyclic amides.

It thus appears that for compounds containing the amide group the tendency to formation of intermolecular hydrogen bonds runs parallel with the contribution of bipolar mesomers



Dielectric constant increments of benzene solutions at 30°.

1, 1-*Methyloxazolid-2-one.*
2, *Oxazolid-2-one.*
3, 6-*Aminohexanoic lactam.*

to the structure of these compounds. A plausible explanation may be that the van der Waals forces operative in the formation of hydrogen bonds between simple amides are augmented in oxazolid-2-one by electrostatic attraction forces between the negative oxygen and the hydrogen atom, to which the positive charge of the nitrogen atom is probably transferred (IX) (cf. Syrkin and Diatkina, " Structure of Molecules and the Chemical Bond," Butterworth Scientific Publ., London, 1950, pp. 274—275).

Experimental

1-*Methyloxazolid-2-one* (D. Ben-Ishai, unpublished results).—This was synthesised from 2-hydroxyethylmethylamine according to Katchalski and Ben-Ishai (*J. Org. Chem.*, 1950, **15**, 1067). The colourless oily *lactam* distilled at 86—88°/3 mm. and had n_D^{25} 1·454 and d_4^{25} 1·170 (Found: C, 47·4; H, 7·4; N, 13·9. $C_4H_7O_2N$ requires C, 47·5; H, 7·0; N, 13·85%). The molar refraction was R_D 23·4 ml. From bond refractions (Vogel, Cresswell, Jeffery, and Leicester, *J.*, 1952, 514) a value of 24·1 ml. is calculated. Similar negative values for R_D (obs.) $-R_D$ (calc.) have been reported for other five-membered heterocyclic compounds (Bergmann *et al.*, *loc cit.*).

Oxazolid-2-one.—This was prepared and purified according to Katchalski and Ben-Ishai (*loc. cit.*) and had m. p. 89—90°.

6-Aminohexanoic Lactam.—A commercial product was recrystallized several times from heptane. The colourless leaves had m. p. 65—66°.

The measurement of densities and dielectric constants, as well as the calculation of the dipole moments from the slope of the linear plots of these quantities *versus* weight fraction, have been described elsewhere (Fischer, *J. Chem. Physics*, 1951, **19**, 395).

Dipole moments were calculated from results of measurements at weight fractions below 0·0005.

A rough calculation shows that in a 0·6% (by wt.) solution of oxazolidone in benzene about 70% of the solute is dimerized. No attempt has been made to determine the dimerisation constant accurately at these high degrees of association.

The author thanks Dr. E. D. Bergmann for his interest, and Dr. Dov Ben-Ishai for samples of oxazolidones.

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870. *Assay and Degradation of* ^{14}C-*Labelled Choline.*

By H. R. V. ARNSTEIN.

DURING work on the biosynthesis of choline from ^{14}C-labelled precursors by the rat, the amount of ^{14}C in the methyl groups and ethanolamine moiety of choline had to be estimated separately. For this purpose choline chloroplatinate is usually oxidised with alkaline permanganate to trimethylamine, which is isolated as the chloroplatinate (du Vigneaud, Cohn, Chandler, Schenk, and Simmonds, *J. Biol. Chem.*, 1941, **140**, 625). The radioactivity in the trimethylamine chloroplatinate should correspond with the amount of ^{14}C in the methyl groups of choline and the radioactivity in the ethanolamine moiety can then be calculated by difference.

However, in some experiments, particularly when the choline solution was heated vigorously during the permanganate oxidation, inconsistent results were obtained and the degradation procedure was therefore checked with synthetic choline labelled with ^{14}C in the methyl groups. It was again found that the radioactivity of the " trimethylamine " chloroplatinate was variable and in one experiment was only 16% of the calculated value. This chloroplatinate sample was converted into the free base which was analysed by vapour-phase partition chromatography (James, Martin, and Smith, *Biochem. J.*, 1952, **52**, 238), kindly carried out by Dr. A. T. James. It was found that the supposed trimethylamine consisted of ammonia 86% and trimethylamine only 14%, the latter value being in good agreement with the observed radioactivity of the chloroplatinate. It is also of interest that the mixture appeared to contain neither mono- nor di-methylamine.

In further experiments the " trimethylamine " chloroplatinate fraction was converted into barium carbonate by wet combustion (cf. Van Slyke and Folch, *J. Biol. Chem.*, 1940, **136**, 509) and the radioactivity of the choline-methyl groups was calculated from the radioactivity of the barium carbonate.

Radioactivity of synthetic ^{14}C-*methyl-labelled choline and degradation products.*

Compound	Radioactivity (μc/mole) * Exp. I	Exp. II
Choline chloroplatinate	4·2	2·8
" Trimethylamine " chloroplatinate	2·8	2·4
$BaCO_3$ obtained by wet combustion of " trimethylamine " chloroplatinate	0·73	0·48
Methyl groups of choline (calc. from radioactivity of $BaCO_3$)	4·4	2·8

* Standard error ±3%.

The Table shows that there is good agreement between the observed radioactivity of the choline chloroplatinate and the value calculated from the barium carbonate derived from the " trimethylamine " chloroplatinate and it is suggested that combustion of the " trimethylamine " is essential for reliable results.

For the assay of choline itself, however, the wet combustion procedure of Van Slyke and Folch (*loc. cit.*) was found to be unsatisfactory. When synthetic ^{14}C-methyl-labelled

choline (specific activity : 650 μc per g. of carbon) was oxidised by this method, the carbon dioxide, isolated as barium carbonate, contained only 52% of the theoretical radioactivity (340 μc per g. of C, here and in all cases). As difficulties in obtaining complete combustion of, for example, the xanthhydryl derivative of urea have been reported (Armstrong, Singer, Zbarsky, and Dunshee, *Science*, **1950, 112,** 531), it seemed likely that the above result was due to the incomplete combustion of the methyl groups of choline. This was confirmed by oxidising choline labelled with ^{14}C in the ethanolamine moiety and collecting the carbon dioxide in fractions. The specific radioactivity of the choline chloroplatinate was 3·4 μc per g. of carbon, which was unchanged after conversion into the mercuric chloride complex (3·52 μc). The specific radioactivities of the first two fractions of carbon dioxide from the wet combustion of this material were 5·9 and 5·8 μc respectively. Carbon dioxide evolution then ceased and a further quantity of fresh oxidation mixture had to be added. The carbon dioxide which was then evolved had a specific radioactivity of 0·75 μc.

It is obvious from the above results that complete combustion of the sample is essential for accurate radioactivity estimations of ^{14}C-labelled choline as barium carbonate and it is more convenient to measure the radioactivity of the chloroplatinate directly.

Experimental

Radioactivity Determinations.—The measurements were carried out on " infinite thickness " samples, *i.e.*, 25 mg. or more of material per sq. cm., mounted on 1-sq. cm." Polythene " discs, as described by Popják (*Biochem. J.*, 1950, **46**, 560). Samples were counted with a helium-filled bell-shaped Geiger–Müller counter which had a thin mica window. The " background " of the instrument was about 8 counts/min. and a sample which contained 1 μc of ^{14}C per g. of substance gave aprox. 1000 counts/min. when counted as described above.

Preparation of Choline Chloride Labelled with ^{14}C in the Ethanolamine Moiety.—The synthesis of this compound from $^{14}CH_3{\cdot}CO_2Na$ (obtained from the Radiochemical Centre, Amersham) has already been described (Arnstein, *Biochem. J.*, 1951, **48**, 27). The choline contained no ^{14}C in the carbinol-carbon atom (D. B. Sprinson, private communication) and the reaction of trimethylamine with ethylene chlorohydrin therefore does not involve the intermediary formation of ethylene oxide. The choline was assayed both as the chloroplatinate (3·4 μc per g. of carbon) and the mercuric chloride complex (3·5 μc).

Preparation of [^{14}C-methyl]Choline Chloride.—[^{14}C-methyl]Choline iodide, prepared by the reaction of $^{14}CH_3I$ with dimethylaminoethanol essentially as described by Roe (*Elisha Mitchell Sci. Soc.*, 1951, **67**, 54) was dissolved in water and converted into the chloride by addition of excess of aqueous silver acetate, followed by excess of 2N-hydrochloric acid. The silver halides were removed by centrifuging and the solution of choline chloride was evaporated to dryness *in vacuo*. For assay, this material was converted into the chloroplatinate.

Wet Combustion of Samples.—Approx. 30—50 mg. of choline chloroplatinate (6—10 mg. of C) were heated with the oxidation mixture (2—5 ml.) described by Van Slyke and Folch (*loc. cit.*) in a tube through which carbon dioxide-free nitrogen was slowly passed. The exit gases were bubbled through approx. 10—20 ml. of saturated barium hydroxide solution. The barium carbonate was collected, washed twice with carbon dioxide-free distilled water, twice with ethanol, and once with ether, and dried at 100°.

Oxidation of Choline to Trimethylamine.—Choline chloroplatinate was oxidised with alkaline potassium permanganate as described by du Vigneaud *et al.* (*loc. cit.*; cf. Lintzel and Monasterio, *Biochem. Z.*, 1931, **241**, 273) in a flask through which carbon dioxide was passed, the alkaline solution of choline being warmed to about 60—100° before the permanganate was added. The trimethylamine was absorbed in two traps which contained 0·3N-hydrochloric acid. The hydrochloric acid was evaporated *in vacuo*. The residue was dissolved in ethanol, and a solution of chloroplatinic acid in ethanol was added. The trimethylamine chloroplatinate was collected, washed with alcohol and ether, and dried at 100°.

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871. *The Preferential Reduction of Nitro-groups in Polynitro-compounds. Part V.* 1 : 3 : 6-, 1 : 3 : 8-, and 1 : 4 : 5-Trinitronaphthalene.*

By E. R. Ward and L. A. Day.

Previous work in this field (Hodgson *et al.*, Part I, *J.*, 1943, 318; Part II, *J.*, 1945, 454; Part IV, *J.*, 1945, 794; cf. *J.*, 1949, 1187) has shown that preferential reduction of polynitronaphthalenes occurs at α-positions with acid stannous chloride and at β-positions with alkaline sulphides. The production of 4 : 5-dinitro-2-naphthylamine from 1 : 3 : 8-trinitronaphthalene with sodium hydrogen sulphide and 3 : 6-dinitro-1 : 8-naphthylenediamine from 1 : 3 : 6 : 8-tetranitronaphthalene with acid stannous chloride did not, however, have the same significance as reductions of the dinitronaphthalenes since these reaction products represented considerably less than half of the starting materials. Working under similar reaction conditions we have now investigated the reduction of 1 : 3 : 6-, 1 : 3 : 8-, and 1 : 4 : 5-trinitronaphthalenes.

By reaction with acid stannous chloride 1 : 3 : 6-trinitronaphthalene affords a 25% yield of the expected 3 : 6-dinitro-1-naphthylamine, the latter being orientated by deamination to the known 2 : 7-dinitronaphthalene. Despite considerable variation in procedure only very small amounts of amine could be isolated in reductions of this compound with sodium hydrogen sulphide, the main reaction appearing to be replacement of one or more nitro-groups by sulphur-containing radicals. The yield of basic product was insufficient to merit further investigation, and in any case the result would be of little theoretical significance.

Unsuccessful attempts to reduce 1 : 3 : 8-trinitronaphthalene with acid stannous chloride have already been reported (Ward, Thesis, London Univ., 1946) and further attempts have failed to produce a significant amount of reduction product capable of purification.

With stannous chloride 1 : 4 : 5-trinitronaphthalene gave a very small yield of what appeared to be a mixture of two amines, and with sodium hydrogen sulphide gave a very small yield of an amine not identical with 4 : 8-dinitro-1-naphthylamine. The main product in the latter case appeared to be sodium 4 : 8-dinitro-1-naphthyl sulphide, this being confirmed by its reaction with *o*-dinitrobenzene to give a compound identical with that given by the reaction of sodium *o*-nitrothiophenoxide with 1 : 4 : 5-trinitronaphthalene. Both sulphides are presumably 4 : 8-dinitro-1-*o*-nitrophenylthionaphthalene on analogy with the product arising from 1 : 4 : 5-trinitronaphthalene and sodium *o*-nitrothiophenoxide (Hodgson and Ward, *J.*, 1948, 2017). As expected neither 1 : 3 : 6- nor 1 : 3 : 8-trinitronaphthalene would react with sodium *o*-nitrothiophenoxide.

It is convenient to report here that 1 : 4 : 5 : 8-tetranitronaphthalene in reaction with this reagent afforded a compound which is probably 4 : 8-dinitro-1 : 5-di-*o*-nitrophenylthionaphthalene, simultaneous replacement of two mobile nitro-groups occurring.

Experimental.

Analyses are by Drs. Weiler and Strauss, Oxford.

Reductions with Stannous Chloride.—The trinitronaphthalene (10 g.), suspended in acetic acid (40 c.c.), was treated, with stirring, with a solution of hydrated stannous chloride (25 g.) in acetic acid (60 c.c.) saturated with dry hydrochloric acid. The rate of addition was such as to keep the temperature at 25—30° (*ca.* 30 minutes). The mixture was stirred for a further 30 minutes and then as much acetic acid as possible (*ca.* 70—80 c.c.) removed by distillation *in vacuo*. The residue was poured on ice and basified with aqueous sodium hydroxide (20%). The crude product was extracted with warm dilute hydrochloric acid and reprecipitated with ammonia at 0°.

1 : 3 : 6-Trinitronaphthalene gave 3 : 6-*dinitro*-1-*naphthylamine* (2·2 g., 25%), red-orange needles, m. p. 270—272°, from ethanol (Found : N, 18·4. $C_{10}H_7O_4N_3$ requires N, 18·0%).

1 : 4 : 5-Trinitronaphthalene gave a mixture of red and yellow needles, m. p. 130—140° (0·2 g.), not separated by crystallisation from ethanol; a large amount of black tar was also obtained.

* Part IV, *J.*, 1945, 794.

Orientation of 3 : 6-*Dinitro*-1-*naphthylamine*.—The amine (1 g.), dissolved in sulphuric acid (5 c.c.; *d* 1·84), was stirred into a solution of sodium nitrate (0·4 g.) in sulphuric acid (2 c.c.; *d* 1·84). The mixture was then added slowly to acetic acid (14 c.c.) below 20°. After 30 minutes the diazonium solution was added rapidly to methanol (50 c.c.) containing suspended cuprous oxide (5 g.). After 15 minutes' stirring the mixture was poured into ice-water (100 c.c.), and the solids were filtered off, washed with water, and extracted portionwise with hot ethanol (100 c.c. in all). The extract on concentration deposited 2 : 7-dinitronaphthalene, which, recrystallised from ethanol, had m. p. 232° alone or admixed with an authentic specimen.

Reductions with Sodium Hydrogen Sulphide.—The trinitronaphthalene (2 g.) was suspended in methanol (30 c.c.) with sodium hydrogen carbonate (0·4 g.) and reduced by the addition of aqueous methanolic sodium hydrogen sulphide (Hodgson and Ward, *J.*, 1948, 242; 1·5 mols.) during 15 minutes. Reaction was continued a further 15 minutes, the mixture added to ice-water (150 c.c.), and the solid separated, washed with water, and extracted with warm dilute hydrochloric acid. The extracts were basified at 0° with ammonia.

1 : 3 : 6-Trinitronaphthalene gave only a very small amount of yellow-brown amine on basification, the reaction liquors on acidification giving a black tar which could not be purified. 1 : 4 : 5-Trinitronaphthalene gave a small amount of an orange amine (0·1 g.), which, crystallised from ethanol, had m. p. 180—190° (mixed m. p. with 4 : 8-dinitro-1-naphthylamine 140°). The reaction liquor gave a grey precipitate on acidification. This was dissolved in methanol (5 c.c.) containing sodium hydroxide (0·1 g.), and the solution filtered to remove tar and added dropwise to a solution of *o*-dinitrobenzene (1 g.) in methanol (5 c.c.) under reflux. After 10 minutes the mixture was cooled and the black reaction product separated. Recrystallised from acetic acid (charcoal) it had m. p. 190° unchanged by admixture with 4 : 8-dinitro-1-*o*-nitrophenylthionaphthalene. Variations of procedure with these trinitronaphthalenes, *e.g.*, reaction at room temperature over long periods, altering the amount of sodium hydrogen carbonate, using other sulphides of sodium, failed to improve the yields of amines.

Reaction of Polynitronaphthalenes with Sodium o-*Nitrothiophenoxide*.—1 : 4 : 5-Trinitronapthalene (0·5 g.) suspended in ethanol (20 c.c.) was treated with *o*-nitrothiophenol (0·3 g.) and sodium hydroxide (0·1 g.) in ethanol (1·5 c.c.) After 10 minutes' refluxing the mixture was cooled and the solid 4 : 8-*dinitro*-1-*o*-*nitrophenylthionaphthalene* (0·3 g.) filtered off. Recrystallised from acetone, then from acetic acid, this had m. p. 190° (Found: S, 8·2. $C_{16}H_9O_6N_3S$ requires S, 8·6%).

Under similar reaction conditions 1 : 3 : 6-, and 1 : 3 : 8-trinitronaphthalenes gave no solid reaction product and the reaction mixture contained no liberated nitrite.

4 : 8-*Dinitro*-1 : 5-*di*-o-*nitrophenylthionaphthalene*. 1 : 4 : 5 : 8-Tetranitronaphthalene (0·5 g.), suspended in ethanol (20 c.c.) similarly treated, gave 4 : 8-*dinitro*-1 : 5-*di*-o-*nitrophenylthionaphthalene* (0·5 g.), m. p. 305—307° (from acetic acid) (Found: N, 10·7; S, 12·2. $C_{22}H_{12}O_8N_4S_2$ requires N, 10·6; S, 12·2%).

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872. *The Rate of Nucleation of Ammonium Iodide on Mica.*

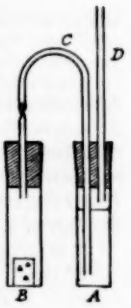
By R. S. Bradley.

The ideal method of studying two-dimensional nucleation and crystal growth would be to prepare a large perfect crystal surface and to study at what degree of supersaturation growth proceeds. This is not normally possible, since the large crystals have grown in all probability by Frank's dislocation mechanism (*Phil. Mag. Suppl.*, **1952, 1, 91**), and no surface nucleation of the classical type required for a perfect surface will be necessary. It was hoped to overcome this difficulty by growing ammonium iodide on a mica substrate, comparatively large patches of which are molecularly perfect although there are many steps (Tolansky, " Multiple beam interferometry of surfaces and films," Oxford Univ.

Press, 1948) and occasional points of emergence of dislocation vectors (Amelinckx, *Nature*, 1952, **169**, 580).

Experimental

Ammonium iodide grows with the 111 face parallel to the mica and appears as oriented prisms (Friedel, " Leçons de cristallographie," Paris, 1926). The apparatus used to detect the appearance of these prisms consisted of two specimen tubes *A* and *B*, 1 cm. in diameter (Figure) with thin glass walls. *A* and *B* were fitted with rubber bungs and were joined by a glass tube C in which there was a constriction holding a small pellet of compressed filter paper. Tube *A* was filled with a hot saturated solution of ammonium iodide, and after the apparatus had been assembled with a piece of freshly cleaved mica in *B* the tubes were immersed in a thermostat at 30—50°, with the narrow tube *D* emerging from the thermostat liquid surface. The hot solution of ammonium iodide was cooled and rapidly attained equilibrium. After the apparatus had remained in the thermostat for an hour, with constant shaking, tube *D* was attached to a filter pump, and air was removed from *A* and *B*. On the release of the pump the saturated solution was forced into *B* and was filtered from micro-crystals and particulate matter. The apparatus was raised until the rubber bungs just protruded from the thermostat liquid, water was wiped off, and tube *B* was removed and closed by a stopper carrying a solid glass rod for convenience of clamping. Tube *B* was then plunged, still stoppered, into water at 60—70°, in order to destroy any micro-crystalline nuclei which had escaped filtration, and after 30 minutes was replaced in the thermostat. The latter was then allowed to cool at approx. 1° per hour, and the mica was observed with a lens for the appearance of crystals of ammonium iodide. No significant difference was observed in the results when the rate of cooling was greatly decreased. The temperature of appearance of the crystals was surprisingly sharp and very small crystals could easily be detected by the glinting in the light of a lamp. In so far as the crystals had reached visible size before their appearance was recorded a slight overshooting of the supercooling for nucleation was inevitable, but as judged by the extent to which the crystals grew on further slow cooling and the results with different rates of cooling the overshooting was only of the order 0·1°. A batch of five sets were studied at one time and the whole was repeated many times.



Ammonium iodide solutions decompose slowly, giving small quantities of iodine, but no significant difference was noted between the critical degree of cooling for the crystallisation of brown and colourless solutions. The filter did not appreciably alter the concentration, as was proved by filtering the solution as above and then adding a few mg. of ammonium iodide to the filtrate. Even after the solution had been shaken for an hour in the thermostat the crystal grains had neither grown nor dissolved; since the ammonium iodide dissolved amounted to a few grams, this is a sensitive test. It seemed unlikely that vibration was influencing the rate of crystal nucleation, since the supersaturated solutions deposited crystals only on violent shaking, and then in a dense cloud which was deposited on the glass and on the mica.

Some 40—50 observations were made at each of the initial temperatures 48·5° and 31·5°. The critical supercooling was 1·85° and 1·45°, and the standard deviation 0·24° and 0·13°, respectively. These degrees of supercooling correspond to a supersaturation ratio (concentration/solubility) of 1·008 and 1·007 at 46·65° and 30·05°, respectively (cf. Seidell, " Solubilities of inorganic and metal compounds," van Nostrand, 1940). In view of the small effect of temperature on the critical supercooling, readings at intermediate temperatures were not taken.

Discussion

In order that a perfect crystal face may grow in a supersaturated solution a nucleus of the critical size must be formed. The number of molecules n_c in the critical nucleus is given by

$$n_c^{\frac{1}{2}} = \eta g/(2kT \ln \alpha)$$

where η is the edge energy per molecule, g a packing factor such that the number of molecules in the edge of a nucleus containing n_c molecules is $gn_c^{\frac{1}{2}}$, k the Boltzmann constant, T the absolute temperature, and α the supersaturation ratio (Frank, *loc. cit.*; Bradley, *Quart. Reviews*, 1951, **5**, 315). In these experiments, η refers to the edge of an ammonium iodide crystal resting on mica and surrounded by solution. When mica is cleaved the potassium

ions probably divide equally between the two faces, forming a hexagonal arrangement of two-dimensional lattice points, half of which are occupied by potassium and half by negative holes. It seems likely that the nucleus of ammonium iodide could be formed on a suitable patch consisting largely of either potassium ions or negative holes, so that the nucleus is made up of a layer of cations and a layer of anions, one of which lies above the other.

The classical theory of surface nucleation gives for the rate of formation of nuclei in cm.^{2} per sec. the value

$$I = C[\eta g/(8\pi kTn_c^{\frac{1}{3}})]^{\frac{1}{2}} \exp[-\Delta G_{max.}/(kT)]$$

where C is a collision factor, and where

$$\Delta G_{max.} = \tfrac{1}{2}\eta g n_c^{\frac{1}{3}} = \tfrac{1}{2}\eta^2 g^2/(2kT \ln \alpha)$$

According to this result the rate of nucleation is highly dependent on temperature, since $\Delta G_{max.}$ is temperature-dependent. The result is that at a certain degree of supercooling a catastrophic nucleation sets in with an apparently sharp boundary, although theoretically nucleation will occur slowly at much smaller degrees of supercooling. It is usual to take $I = 1$ nucleus per cm^2. per sec. as the criterion for this catastrophe, slightly smaller or larger degrees of supercooling giving much smaller or greater rates, respectively.

It is usually considered in the light of the preceding two equations that surface nucleation would occur from the vapour on a perfect flat crystal surface at values of log α of the order of unity (Frank, *loc. cit.*; *Discuss. Faraday Soc.*, **1949**, **5**, 48, 67). This is in contrast to Volmer and Schultze's experiments with iodine, since the experimental ln α is of the order 0·01 (*Z. physikal. Chem.*, **1931**, *A*, **156**, 1), and the deviation is attributed to growth by a dislocation mechanism (Frank, *loc. cit.*). At first sight the results on ammonium iodide support the view that growth occurs on dislocation edges, since ln $\alpha \sim 0{\cdot}0075$. It seems unlikely, however, that the ammonium iodide could make use of the dislocation edges which are present on the surface, since the molecular step of the mica is much too large. Moreover, the orientation of the prisms of ammonium iodide suggests that the crystallisation is due to true surface nucleation; there are comparatively large patches of the mica which are molecularly plane. It seems more likely that, in contrast to the growth of crystals from the vapour, two-dimensional nucleation may occur from solution on a perfect crystal face at supersaturation ratios near to unity. We may attribute the low results for ammonium iodide to the small value of η, which would have to be approximately a tenth of the value for an iodine crystal growing from the vapour, a not unreasonable result. It seems possible, therefore, that these experiments refer to the unusual case of true two-dimensional nucleation on a perfect crystal face.

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873. *A Preliminary Study of the Main Polysaccharide of* Lupinus termis *Seeds.*

By Wadie Tadros and Mohamed Kamel.

Lupinus termis seeds are commonly used as edible material in Egypt. The same polysaccharide material was obtained on extraction of the powdered skinned seeds by (*a*) a method modified from that used for the extraction of the hemicellulose of the New Zealand flax (*Phormium tenax*) (McIlroy, Holmes, and Mauger, *J.*, **1945**, **796**), or (*b*) the procedure adopted by Hirst, Jones, and Walder (*J.*, 1947, 1225) for extraction of *Lupinus albus*. McIlroy *et al.* used 4% aqueous sodium hydroxide; in the present investigation, the same product was obtained with 0·5%, 1%, or 4% aqueous sodium hydroxide. The polysaccharide is built of D-galactose, L-arabinose, and a uronic acid, which since it affords mucic acid is D- or L-galacturonic acid.

Hirst *et al.* (*loc. cit.*) showed that associated with the galactan of *Lupinus albus* there was an araban which could be partly removed by extraction with 70% alcohol and a pectic acid which could be precipitated as calcium pectate. We failed to obtain an araban or pectic acid from our polysaccharide material.

In estimations of arabinose as its benzoylhydrazone (Hirst, Jones, and Woods, *J.*, 1947, 1048), it was found useful to add a weighed quantity of arabinose (about equal to that expected) which was then subtracted from the value obtained.

Experimental

Extraction.—(*a*) After being soaked overnight in water the seeds (500 g.) were skinned and twice milled. The powder was extracted with water (2 l.) on a shaker for 4 hours and then filtered through muslin. This process was repeated three times. The cake thus obtained was extracted with 0·5% aqueous ammonium oxalate (2 l.) for 6 hours on a boiling-water bath to remove pectic substances (McIlroy *et al.*, *loc. cit.*). The residue, washed and pressed, was stirred with 4% aqueous sodium hydroxide for 12 hours at room temperature and heated on a boiling-water bath for 3 hours. The alkaline extract was filtered through muslin and the extraction was repeated (it was then complete). The combined filtrates were poured into alcohol (4 vols.), and the precipitated polysaccharide was purified by solution in water and reprecipitation by acidified alcohol. The polysaccharide material (A) was washed with alcohol, then ether, and dried in a vacuum at 100° over phosphoric oxide. It was a cream-coloured amorphous powder insoluble in cold water and sparingly soluble in hot water (yield, 10—15 g.) [Found (averages): total furfuraldehyde, 9·6; uronic anhydride, 8·4; araban, 14·3; methoxyl, 0; ash, 0; galactan by difference, 77·3%]. The same product was obtained on using 0·5% or 1% aqueous sodium hydroxide.

(*b*) After being soaked overnight in water, the seeds (500 g.) were stripped of their skins and milled twice. The protein matter was then extracted by stirring them with 10% aqueous sodium chloride for 3 hours, followed by filtration, and repetition of the process three times. The solid residue was then stirred with 0·2% aqueous sodium hydroxide thrice for 12 hours at a time. Addition of hydrochloric acid to the filtrate then gave no precipitate, indicating absence of appreciable quantities of protein. The solid residue was then boiled with 0·2% aqueous sodium hydroxide (2 l.) for 3 hours, after which it was filtered and the filtrate poured into alcohol (4 vols.). The precipitated polysaccharide was filtered off and redissolved in water. The aqueous solution was filtered and the polysaccharide (B) precipitated by addition of acidified alcohol, filtered off, washed until free from acid, and dried in a vacuum over phosphoric oxide at 100°. It was a cream-coloured powder (yield 12 g.) [Found (averages): total furfuraldehyde, 9·6; uronic anhydride, 8·4; araban, 14·3; methoxyl, 0; ash, 0; galactan by difference, 77·3%].

Hydrolysis.—The material A or B (4 g.) was boiled with 4% sulphuric acid (50 c.c.) for 5 hours until the reducing power (Bertrand method; Browne and Zerban, "Sugar Analyses," Chapman & Hall, London, 1948, p. 776) of the solution remained constant. The solution was neutralised with barium carbonate and filtered. The filtrate was concentrated under reduced pressure at 70°, and the syrupy product poured into alcohol (40 c.c.). The precipitated barium salt was filtered off and gave on oxidation with bromine (see below) mucic acid, m. p. 212° not depressed on admixture with an authentic sample. The filtrate was concentrated in vacuum at 70° to 10 c.c. Qualitative analysis showed the presence of arabinose (identified as its benzoylhydrazone, m. p. 190°, and as its diphenylhydrazone, m. p. 204°, both not depressed on admixture with authentic samples) and galactose (identified as its methylphenylhydrazone, m. p. 186° not depressed on admixture with an authentic sample). "Authentic" derivative were prepared from the above sugars.

Quantitative analysis of the hydrolysate (Hirst, Jones, and Woods, *loc. cit.*) gave 13·8% of arabinose and 79·4% of galactose.

Oxidation (cf. Heidelberger and Goebel, *J. Biol. Chem.*, 1927, **74**, 613).—A mixture of the material A or B (1·2 g.), 7·5% hydrobromic acid (12 c.c.), and bromine (0·6 c.c.) was heated on a boiling-water bath for 10 hours. A slight precipitate proved to be mucic acid, m. p. 212° alone or mixed with an authentic sample. On removal of mucic acid, no potassium hydrogen saccharate could be obtained from the filtrate, indicating the absence of glucuronic acid.

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Giza, Egypt. [*Received, July 1st*, 1952.]

874. 5-*Benziloyloxymethylfurfuryltrimethylammonium Chloride.*

By A. S. Bailey, D. H. Bates, and H. R. Ing.

The benzilic esters of choline and analogous alkamines have mydriatic properties (Ford-Moore and Ing, *J.*, 1947, 55) so that the discovery that 5-methylfurfuryltrimethylammonium iodide had intense acetylcholine-like activities (Ing, Kordik, and Tudor-Williams, *Brit. J. Pharmacol.*, 1952, **7**, 103) suggested that analogous compounds with a 5-benzilyloxymethyl group might be mydriatics. 5-Benziloyloxymethylfurfuryltrimethylammonium chloride was prepared but it had negligible activity when tested as a mydriatic in mice by Pulewka's method (see Ing, Dawes, and Wajda, *J. Pharmacol.*, 1945, **85**, 85); moreover, even large doses (2—4 mg.) did not prevent the vasodilator effect of 1 μg. of acetylcholine in the cat.

Experimental.—5-Hydroxymethylfurfuryldimethylamine was prepared as described by Ing, Kordik, and Tudor-Williams (*loc. cit.*), converted into its methiodide, m. p. 129°, and characterized as its *methopicrate*, which crystallized from ethanol, m. p. 125° (Found: C, 45·9; H, 4·9. $C_{15}H_{18}O_9N_4$ requires C, 45·2; H, 4·5%). The methochloride, prepared by means of silver chloride from the methiodide but not isolated, was covered with chloroform and treated with excess of thionyl chloride; after 24 hours at room temperature the reaction mixture was evaporated, finally *in vacuo*, and the 5-chloromethyl derivative characterized as its *picrate* which, crystallized from ethanol, had m. p. 116° (Found: C, 43·4; H, 4·0. $C_{15}H_{17}O_8N_4Cl$ requires C, 43·2; H, 4·1%). The crude methochloride (14·2 g.) was converted by heating with potassium benzilate (4·5 g.) in ethanol into the methobenzilate; removal of potassium chloride and evaporation of the solvent left a gum, which after being heated at 100° for 10 hours and subsequently treated with acetone gave solid *5-benziloyloxymethylfurfuryltrimethylammonium chloride* (cf. Horenstein and Pahlicke, *Ber.*, 1938, **71**, 1654). The crude product, dissolved in ethanol, was passed through a charcoal column and recovered by evaporation of the solvent and treatment of the residue with acetone. The solid so obtained, purified by crystallization from hot acetone in which it was sparingly soluble, had m. p. 154° (decomp.) (Found: C, 65·6; H, 6·3. $C_{23}H_{26}O_4NCl$ requires C, 66·4; H, 6·2%).

5-Hydroxymethylfurfuryldiethylamine, prepared in the same way as the dimethylamino-compound, was converted into its *ethiodide* which, crystallized from ethanol–ethyl acetate, had m. p. 142° (decomp.) (Found: C, 42·7; H, 6·4. $C_{12}H_{22}O_2NI$ requires C, 42·5; H, 6·5%).

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875. 2-3′ : 5′-*Dihydroxyphenylethylamine and* 3 : 5-*Dihydroxyphenylalanine.*

By A. S. Bailey, D. H. Bates, H. R. Ing, and M. A. Warne.

3 : 5-Dihydroxyphenylalanine and its decarboxylation product, 2-3′ : 5′-dihydroxyphenylethylamine, were needed for studies on the substrate specificity of amino-acid decarboxylases (Blaschko, *Biochim. Biophys. Acta*, 1950, **4**, 130); the latter compound was also needed for pharmacological work on isomeric dihydroxyphenylethylamines.

Experimental.—Methylation of 3 : 5-dihydroxybenzoic acid (*Org. Synth.*, 1941, **21**, 27), followed by esterification (best through the acid chloride) and reduction by lithium aluminium hydride, gave 3 : 5-dimethoxybenzyl alcohol, which was readily converted by thionyl chloride and pyridine into 3 : 5-dimethoxybenzyl chloride, m. p. 43—45° (Adams, Mackenzie, and Loewe, *J. Amer. Chem. Soc.*, 1948, **70**, 664; Adams, Harfenist, and Loewe, *ibid.*, 1949, **71**, 1624).

The benzyl chloride (20 g.) in ethanol (50 ml.) was added slowly to a hot solution of potassium cyanide (20 g.) in water (20 ml.), and the mixture heated for 3 hours at 100°. The benzyl cyanide, isolated by extraction with ether, was obtained as a pale yellow solid (Adams, Mackenzie, and Loewe, *loc. cit.*, give m. p. 53°) (yield 85%). The cyanide (11 g.) in ether (100 ml.) was added to lithium aluminium hydride (4 g.) in ether (150 ml.) with stirring. After 1 hour the crude amine was isolated in the usual way and demethylated by slow distillation with

acetic acid (25 ml.), hydriodic acid (*d* 1·5; 25 ml.), and red phosphorus (2 g.). When methyl iodide ceased to distil, the solution was diluted, filtered, and evaporated *in vacuo*. The residue was crystallized repeatedly by slow evaporation of its aqueous solution *in vacuo* over phosphoric oxide, and 2-3′ : 5′-*dihydroxyphenylethylamine hydriodide* obtained as its monohydrate which began to decompose at 185° (Found: C, 32·3; H, 4·5; N, 4·6. $C_8H_{11}O_2N,HI,H_2O$ requires C, 32·1; H, 4·7; N, 4·7%).

3 : 5-Dimethoxybenzyl chloride (3·75 g.) was added to a solution of sodium (0·36 g.) and ethyl acetamidomalonate (3·4 g.) in ethanol. After being boiled for 2·5 hours, the solution was evaporated *in vacuo* and the solid residue treated with ice-water. The solid *ethyl acetamido-3 : 5-dimethoxybenzylmalonate* (6·8 g., 87%), recrystallized from light petroleum (b. p. 60—80°)–benzene, had m. p. 114° (Found: C, 59·9; H, 6·7. $C_{18}H_{27}O_7N$ requires C, 58·9; H, 6·8%). It (5 g.) was hydrolysed with concentrated hydrochloric acid–acetic acid (20 ml. of 1 : 1 by vol.); evaporation of the acid solution gave 3 : 5-*dimethoxyphenylalanine hydrochloride*, which crystallized from ethanol (Found: C, 50·7; H, 6·3. $C_{11}H_{16}O_4NCl$ requires C, 50·0; H, 6·1%). The amino-acid hydrochloride (1 g.) was demethylated by heating it with hydrobromic acid (*d* 1·5; 10 ml.) for 2·5 hours. Evaporation of the acid solution *in vacuo* left a brown residue; its aqueous solution was decolorized by passage through a charcoal column, concentrated, and treated with pyridine, which precipitated 3 : 5-*dihydroxyphenylalanine*. The amino-acid crystallized in prisms when its solution in hot water was cooled (Found: C, 54·5; H, 6·0. $C_9H_{11}O_4N$ requires C, 54·8; H, 5·6%).

DEPARTMENT OF PHARMACOLOGY, OXFORD. [*Received, July 7th*, 1952.]

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876. *Heat of Hydrolysis of Phosphorus Oxychloride and Phosphorus Trichloride.*

By E. NEALE and L. T. D. WILLIAMS.

As a preliminary to a study of the thermochemistry of alkyl halogenophosphinates and related compounds, the heats of hydrolysis of phosphorus oxychloride and phosphorus trichloride have been redetermined, a calorimeter of the Dewar-vessel type similar to that described by Bichowsky (*J. Amer. Chem. Soc.*, 1923, **45**, 2225) being used. The reactions are:

$$POCl_3 + x_1H_2O \longrightarrow H_3PO_4 \text{ aq.} + 3HCl \text{ aq.}$$

and

$$PCl_3 + x_2H_2O \longrightarrow H_3PO_3 \text{ aq.} + 3HCl \text{ aq.}$$

where x_1 and x_2 varied from 2600 to 4300 and 4500 to 7500 respectively. Heats of formation were calculated from the results by using values for $Q_f(H_2O \text{ liq.})$, $Q_f(HCl \text{ aq.})$, $Q_f(H_3PO_4 \text{ aq.})$, and $Q_f(H_3PO_3 \text{ aq.})$ given in "Selected Values of Chemical Thermodynamic Properties" (Nat. Bur. Standards, Washington, 1947). The mean results are given below together with the existing published values taken from Bichowsky and Rossini's "Thermochemistry of Chemical Substances," Reinhold Publ. Corpn., N.Y., 1936 (B. and R.), and the "Selected Values, etc." (N.B.S.). Both sets of published values for heat of formation are derived from J. Thomsen's results on heats of hydrolysis ("Thermochemische Untersuchungen," S. A. Barth, Leipzig, 1882, Vol. II), but the Nat. Bur. Standards' publication uses revised values for heat of formation and solution of the products of hydrolysis.

	New value (kcal. mole^{-1})	B. & R. 1936 (kcal. mole^{-1})	N.B.S. 1947 (kcal. mole^{-1})
$POCl_3$ Qaq.	79·9 ± 0·3	72·2	—
Q_f(L)	144·4	147·1	151·0
PCl_3 Qaq.	67·5 ± 0·3	65·1	—
Q_f(L)	79·6	76·9	81·0

Similar measurements on alkyl-substituted derivatives will be reported later.

The accuracy of our results was not high. Since the materials are sensitive to moisture, it is likely that in earlier work, precautions were inadequate. We used the dry-box technique in handling these materials.

The heat of hydrolysis of phosphorus oxychloride has also been measured independently at Manchester University (Dr. Skinner, personal communication) where results were similar to ours though slightly higher.

Acknowledgments are made to the Chief Scientist, Ministry of Supply, for permission to publish these results.

CHEMICAL DEFENCE EXPERIMENTAL ESTABLISHMENT,
PORTON, NEAR SALISBURY, WILTS.

[*Received, July 14th*, 1952.]

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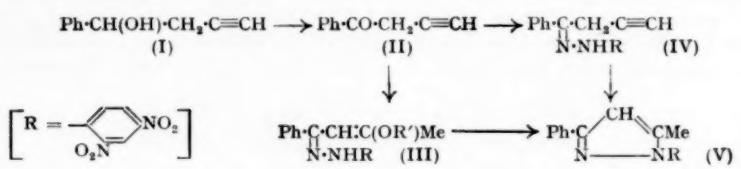
877. *Phenyl Propargyl Ketone.*

By H. B. HENBEST.

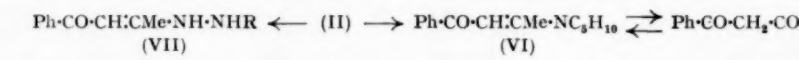
THE modified Reformatsky reaction between benzaldehyde and propargyl bromide in the presence of zinc yields the alcohol (I) (Henbest, Jones, and Walls, *J.*, 1949, 2696). Oxidation of (I) by means of the chromic acid–acetone technique of Bowden, Heilbron, Jones, and Weedon (*J.*, 1946, 39) has been found to give (crystalline) phenyl propargyl ketone (II) in 50% yield, thus providing a convenient route to a member of the little investigated class of β-keto-acetylenic compounds.

Treatment of the ketone with methanolic 2 : 4-dinitrophenylhydrazine sulphate solution afforded a red derivative, shown by analysis to contain a methoxy-group. Since this compound showed maximal light absorption at an appreciably longer wave-length (3910 Å) than acetophenone 2 : 4-dinitrophenylhydrazone (3780 Å), it was evident that it corresponds to structure (III; R′ = Me), the methoxyl group probably contributing to the bathochromic shift as it is attached terminally to the conjugated system (see, *inter al.*, Bowden, Braude, and Jones, *J.*, 1946, 948). With an ethanolic reagent the corresponding ethoxy-derivative (III; R′ = Et) was formed. The (orange) propargyl ketone 2 : 4-



dinitrophenylhydrazone (IV) could be obtained when 95% ethanol or, better, aqueous dioxan was used for the reagent solution. The derivative (IV) gave an insoluble silver salt, and displayed light-absorption properties similar to those of acetophenone 2 : 4-dinitrophenylhydrazone. The compounds (III; R′ = Me or Et) and (IV) were converted into a yellow product when warmed in methanol containing 10% of sulphuric acid. Compared with the 2 : 4-dinitrophenylhydrazones, this was more basic, exhibited no high intensity absorption in the 3700—3900-Å region, and showed no NH stretching frequency in the infra-red spectrum; it is therefore formulated as the pyrazole (V).

Amines such as piperidine do not add rapidly to acetylenic linkages unless there is an adjacent electron-attracting group (cf. addition of amines to α-keto-acetylenes; Bowden, Braude, Jones, and Weedon, *J.*, 1946, 45). However, phenyl propargyl ketone reacted



very rapidly with piperidine to give the piperidino-ketone (VI), previously obtained by Cromwell and Witt (*J. Amer. Chem. Soc.*, 1943, **65**, 308) by heating benzoylacetone with piperidine—as found by these authors, the amine-adduct is very easily hydrolysed to benzoylacetone by dilute acid. It is likely that the relatively ready addition of piperidine to this β-keto-acetylene is due to an initial prototropic change induced by the amine,

forming the isomeric allene-ketone, which would then add piperidine very readily, thus leading to (VI). [A similar mechanism probably operates in the addition of alcohols to give the derivatives (III).] Inductive activation of the triple bond by the keto-group (*via* the methylene group) can be ruled out, because addition of piperidine would then take place in the reverse direction to that observed. Addition of the weaker base, 2 : 4-dinitrophenylhydrazine [to give (VII)], occurred if a small amount of 1-ethylpiperidine was used to effect the initial prototropic change.

Experimental

M.p.s were taken on a Kofler block and are corrected; infra-red spectra were determined with a Perkin–Elmer double beam spectrometer by Dr. G. D. Meakins of this Department.

Phenyl Propargyl Ketone (1-*Phenylbut*-3-*yn*-1-*one*) (II) *and its Derivatives.*—To 1-phenylbut-3-yn-1-ol (14·5 g.) in acetone (70 c.c.) at 5°, chromic acid (7 g.) in sulphuric acid (6 c.c.) and water (20 c.c.) was added dropwise with stirring, the internal temperature being kept at 5°. The mixture was then stirred at 20° for 10 minutes, and the ketone isolated with ether. The crude solid product was triturated with methanol–water (3 : 2), to give almost pure ketone (7·5 g.), m. p. 75—83°. Recrystallization from light petroleum (b. p. 60—80°) gave *phenyl propargyl ketone*, m. p. 78—82° (Found: C, 83·0; H, 5·4. $C_{10}H_8O$ requires C, 83·3; H, 5·6%). Light absorption in ethanol: Max., 2450 Å; $\varepsilon = 12{,}700$ (for acetophenone, Ley and Wingchen, *Ber.*, 1934, **67**, 501, give max., 2400 Å; $\varepsilon = 13{,}200$). Infra-red absorption (on the supercooled melted solid): 3290 (medium strength; $C{\equiv}\overleftrightarrow{C{-}H}$ stretching frequency) and 1690 cm.$^{-1}$ (strong; $\overleftrightarrow{C{=}O}$ stretching frequency). Addition of ammoniacal silver nitrate solution to an alcoholic solution of the ketone precipitated a pale yellow silver derivative, further confirming the presence of a terminal ethynyl group. The ketone was unstable towards alkali (*e.g.*, soft glass), and was best kept in a Pyrex tube at 0°.

The ketone (0·3 g.) in methanol (5 c.c.) was added to 2 : 4-dinitrophenylhydrazine reagent [20 c.c. of a solution prepared by dissolving the base (2 g.) in sulphuric acid (7 c.c.) and methanol (100 c.c.)] at 20°. After a minute an orange solid began to separate and the mixture was then kept at 0° for 1 hour. Water and benzene were added, and the benzene solution was chromatographed on alumina (P. Spence, Grade H). The main band was eluted with benzene, and the product recrystallized from ethyl acetate–methanol (1 : 1), to give 3-*methoxy*-1-*phenylbut*-2-*en*-1-*one* 2 : 4-*dinitrophenylhydrazone* (III; R′ = Me) as orange-red needles (changing to vermilion prisms when left overnight in contact with the mother liquor), m. p. 175—176° (Found: C, 57·4; H, 4·5; OMe, 8·5. $C_{17}H_{16}O_5N_4$ requires C, 57·3; H, 4·55; OMe, 8·7%). Light absorption (in chloroform): Max., 3910 Å; $\varepsilon = 26{,}500$; Min., 3220 Å; $\varepsilon = 3800$. Infra-red spectrum (in Nujol): NH stretching frequency at 3275 cm.$^{-1}$.

Substitution of ethanol for methanol in the preparation of the 2 : 4-dinitrophenylhydrazone gave the corresponding *ethoxy*-derivative (III; R′ = Et) crystallizing from dioxan–ethanol (1 : 1) as vermilion leaflets, m. p. 166—168° (Found: C, 58·5; H, 4·9. $C_{18}H_{18}O_5N_4$ requires C, 58·35; H, 4·9%). Light absorption (in chloroform): Max., 3910 Å; $\varepsilon = 28{,}400$; Min., 3220 Å; $\varepsilon = 3600$.

A solution of the propargyl ketone (0·2 g.) in dioxan (10 c.c.) was added to 2 : 4-dinitrophenylhydrazine (0·3 g.) dissolved in 2N-hydrochloric acid (100 c.c.). A flocculent yellow precipitate formed quickly; after 15 minutes sufficient benzene was added to dissolve the separated solid. The benzene layer was evaporated under reduced pressure to *ca.* 30 c.c., most of the propargyl derivative being precipitated. Recrystallization from ethyl acetate afforded *phenyl propargyl ketone* 2 : 4-*dinitrophenylhydrazone* (IV) as small orange needles, m. p. 193—195° (Found: C, 59·1; H, 3·65. $C_{16}H_{12}O_4N_4$ requires C, 59·25; H, 3·75%). Light absorption (in chloroform): Max., 3760 Å; $\varepsilon = 27{,}200$; Min., 3120 Å; $\varepsilon = 3600$ (cf. light absorption of acetophenone 2 : 4-dinitrophenylhydrazone in chloroform: Max., 3780 Å; $\varepsilon = 28{,}000$; Min., 3140 Å; $\varepsilon = 3500$). Infra-red spectrum (in Nujol): NH stretching frequency at 3280 cm.$^{-1}$. An orange gelatinous precipitate formed immediately when a solution of silver nitrate in methanol was added to a solution of the derivative in dioxan, confirming the presence of a terminal ethynyl group (2 : 4-dinitrophenylhydrazones not containing such a group do not give a precipitate).

A solution of each of the foregoing derivatives (50 mg.) in methanol (4 c.c. containing 10% of sulphuric acid) was heated under reflux for 1 minute. In each case, the solution became very pale yellow. Benzene and aqueous potassium hydrogen carbonate solution were added and the

product was purified by chromatography. Recrystallization from ethanol afforded in each case a good yield of 1-(2 : 4-*dinitrophenyl*)-5-*methyl*-3-*phenylpyrazole* (V) as lemon-yellow plates, m. p. 153—154° (Found : C, 59·25; H, 4·0. $C_{16}H_{12}O_4N_4$ requires C, 59·25; H, 3·75%). Light absorption (in ethanol) : Max., 2460 and 3350—3500 Å; ε = 24,400 and 8100; Min., 2880 Å; ε = 6000. Infra-red spectrum (in Nujol) : NH stretching band at *ca.* 3300 cm.$^{-1}$ absent.

Addition of Piperidine to (II).—Addition of piperidine (250 mg.) to the ketone (250 mg.) in dry ether (6 c.c.) occurred exothermally, and after 5 minutes the solvent was removed under reduced pressure, to give a solid product. Recrystallization from light petroleum (b. p. 60—80°)–benzene (4 : 1) gave the adduct (VI) (320 mg.) as prisms, m. p. 99°, undepressed on admixture with a sample prepared by Cromwell and Witt's method (*loc. cit.*). Light absorption : Max., 2480 and 3400 Å; ε = 10,500 and 26,500 respectively. Bowden, Braude, and Jones (*J.*, 1946, 948) give for the light absorption of the related compound, Ph·CO·CH:CH·NEt_2, Max., 2430 and 3430 Å (ε = 12,000 and 26,000 respectively).

Addition of 2 : 4-*Dinitrophenylhydrazine to* (II).—1-Ethylpiperidine (1 drop) was added to a solution of phenyl propargyl ketone (0·3 g.) and 2 : 4-dinitrophenylhydrazine (0·35 g.) in dry dioxan (20 c.c.). After 2 days at 20° about half of the solvent was removed under reduced pressure, water (2 c.c.) was added, and the mixture kept at 0° overnight. The solid which had separated was crystallized from ethyl acetate–methanol (1 : 1), to yield 3-(2 : 4-*dinitrophenylhydrazino*)-1-*phenylbut*-2-*en*-1-*one* (VII) (0·28 g.) as flat red needles, m. p. 157—158° (a second crystalline form was obtained from the mother-liquors as orange-red plates, showing identical m. p. and light absorption characteristics) (Found : C, 56·05; H, 4·25. $C_{16}H_{14}O_5N_4$ requires C, 56·15; H, 4·1%). Light absorption in chloroform : Max., 3620 Å; ε = 21,600; Min., 2980 Å; ε = 3000. Infra-red spectrum (in Nujol) : NH stretching at 3340 cm.$^{-1}$; C=O stretching at 1685 cm.$^{-1}$ (no absorption bands were shown in the 1650—1750 cm.$^{-1}$ region by the 2 : 4-dinitrophenylhydrazones described above).

THE UNIVERSITY, MANCHESTER, 13. [*Received, July 16th*, 1952.]

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878. *The Preparation of Silver Tetrafluoroborate and Silver*(I) *Fluoride.*

By A. G. SHARPE.

PREVIOUS attempts to make anhydrous silver fluoroborate have all failed (see Booth and Martin, "Boron Trifluoride and its Derivatives," John Wiley and Sons, 1949; Warf, Abstr., XIIth Meeting, Int. Congr. Pure and Applied Chem., New York, 1951). Woolf and Emeléus (*J.*, 1950, 1050) showed that bromine trifluoride converts borax into sodium tetrafluoroborate, and by the action of this reagent on silver borate silver tetrafluoroborate has now been prepared.

Silver fluoroborate is strikingly similar to silver perchlorate, the remarkable properties of which are summarised by Sidgwick ("The Chemical Elements and their Compounds," Oxford Univ. Press, 1950). It is deliquescent, very soluble in water, ether, and toluene, moderately soluble in benzene and *cyclo*hexene, and insoluble in *cyclo*hexane; these observations indicate π-bond formation between the aromatic or unsaturated compounds and the silver ion, similar to that found in the silver perchlorate–benzene complex by Rundle and Goring (*J. Amer. Chem. Soc.*, 1950, **72**, 5337). With iodine, silver fluoroborate forms a powerful iodinating mixture analogous to iodine and silver perchlorate (Birckenbach and Goubeau, *Ber.*, 1932, **65**, 395; Haszeldine and Sharpe, *J.*, 1952, 993). The stoicheiometry of the very fast reaction between iodine, silver fluoroborate, and phenol indicates that it proceeds according to the equation $C_6H_5{\cdot}OH + I_2 + AgBF_4 = C_6H_4I{\cdot}OH + AgI + HF + BF_3$. Toluene and ether are also attacked by the mixture at room temperature; the relative rates of attack (measured by the loss in oxidising power of the solution) show that iodine and silver fluoroborate form an iodinating mixture about as powerful as iodine and silver perchlorate, and considerably more powerful than iodine and silver trifluoroacetate (Haszeldine and Sharpe, *loc. cit.*).

Thermal decomposition of silver fluoroborate into argentous fluoride and boron

trifluoride takes place rapidly at 200°. Treatment of silver borate with liquid bromine trifluoride, followed by heating of the product at this temperature, therefore affords a rapid method for the preparation of small quantities of dry argentous fluoride for use in halogen-exchange reactions; the entire preparation may be carried out in quartz apparatus.

Experimental

Dry silver borate, prepared from silver nitrate and boric acid, was treated with bromine trifluoride as described by Sharpe and Emeléus (*J.*, 1948, 2135). The white residue of *silver tetrafluoroborate*, insoluble in bromine trifluoride, gave only a trace of silver bromide (derived from silver tetrafluorobromite, $AgBrF_4$, present as an impurity) on addition of water. Soluble silver was determined as chloride, and BF_4^- as the nitron salt (Lange, *Ber.*, 1926, **59**, 210) (Found: Ag, 54·5; BF_4, 44·0. $AgBF_4$ requires Ag, 55·3; BF_4, 44·7%). The salt decomposed without melting at 200° when heated in a flask attached to a vacuum line, giving an orange residue of argentous fluoride containing only a little silver bromide (Found: Ag, 83·0. Calc. for AgF: Ag, 85·3%). An *X*-ray powder photograph of the residue showed it to have a face-centred cubic lattice with $a = 4{\cdot}94$ Å; Ott (*Z. Krist.*, 1926, **63**, 222) found $a = 4{\cdot}92$ Å for a sample made from the oxide and hydrofluoric acid. Decomposition of silver tetrafluorobromite under identical conditions does not yield a homogeneous product; some silver difluoride appears to be formed, and there is marked attack on the reaction vessel.

Iodine (0·182 g., 0·72 m-mole) and phenol (0·072 g., 0·75 m-mole) in "AnalaR" benzene were added to silver fluoroborate (0·139 g., 0·72 m-mole) in the same solvent, which is iodinated much less readily than phenol. The colour of iodine at once disappeared, and a gas which fumed strongly in moist air was liberated. The solution was immediately filtered on a Gooch crucible; the filtrate did not liberate iodine from aqueous potassium iodide; the precipitated silver iodide weighed 0·159 g. (0·68 m-mole).

A solution of silver fluoroborate (0·154 g., 0·79 m-mole) and phenol (2 g., excess) in toluene was titrated with a standard solution of iodine in toluene until the colour of iodine appeared in the solution; this end-point corresponded to addition of 0·190 g. (0·75 m-mole) of iodine. The solution was at once filtered, and silver iodide (0·186 g., 0·79 m-mole) equivalent to all of the silver and to one-half of the iodine taken was obtained. These results are similar to those previously obtained with silver perchlorate and silver trifluoroacetate.

University Chemical Laboratory, Cambridge. [*Received, July 16th*, 1952.]

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879. *The Action of Methylmagnesium Iodide on Two Nitramines.*

By Alex. H. Lamberton.

One mol. of gas was immediately evolved when ethereal methylmagnesium iodide was added to an equimolar quantity of methylnitramine in ether. An attempt to alkylate the crude reaction product failed: some methylnitramine was recovered. No gas was evolved in a reaction with nitromorpholine; instead, a solid addition compound (1 : 1) was precipitated in excellent yield. Reduction of this complex with zinc and hydrochloric (or acetic) acid, followed by distillation from an alkaline medium, yielded mixed volatile bases, of which only morpholine was identified. In general it appeared that methylnitramine reacted simply as an acid, whilst the secondary nitramine behaved in a manner more appropriate to *C*-nitro-compounds (Buckley, *J.*, 1947, 1492). No evidence, however, was obtained of the formation of methylmorpholinylhydrazine by reduction of the addition complex.

Experimental.—Ethereal methylmagnesium iodide (20 ml.; containing 17 ± 1 mmoles, determined according to Gilman *et al.*, *J. Amer. Chem. Soc.*, 1923, **45**, 153) was added, in a closed system, dropwise in 15 minutes at 17° to a stirred solution of methylnitramine (16·9 mmoles in 30 ml. of ether), giving a semi-solid precipitate. The gas (17·2 ± 0·5 mmoles), evolved concurrently with the addition, passed through a sulphuric acid bubbler and was measured by displacement of water.

Addition of methyl iodide (17 mmoles in 10 ml. of ether) and subsequent refluxing for 2 hours produced no apparent change in the precipitate. Next morning the salt was decomposed by 2N-hydrochloric acid (20 ml.). No neutral material was obtained on working up, but crude methylnitramine (6·7 mmoles; coloured, but of m. p. 35—37°, undepressed by mixture with authentic material) was recovered from a sodium hydroxide extract of the ethereal layer.

Ethereal methylmagnesium iodide (20 ml.; containing 22·5 mmoles) was added similarly in 25 minutes to 4-nitromorpholine (22·7 mmoles in 40 ml. of ether). Less than 1 mmole gas was evolved. The 1 : 1 addition *complex* precipitated (6·11 g., 90%) was collected, washed with ether, and dried *in vacuo* (Found: C, 19·6; H, 4·5; Mg, 8·0. $C_4H_8O_3N_2,CH_3MgI$ requires C, 20·1; H, 3·7; Mg, 8·1%). On storage *in vacuo* the main bulk of this hygroscopic material remained colourless, but the surface exposed to light became yellow.

The addition complex (10 mmoles) was heated on the water-bath for 2 hours with granulated zinc (7·5 g.) and 5N-hydrochloric acid (60 ml.). After basification with sodium hydroxide the volatile bases liberated (9·3 milliequivs.) were steam-distilled into standard hydrochloric acid. Evaporation of the distillate yielded a mixture of hydrochlorides (Equiv., by weight of solid per equiv. of base, 104; by determination of Cl′, 98), and attempts to isolate a pure salt by crystallisation were unsuccessful. By the Schotten–Baumann reaction the crude material gave 4-toluene-*p*-sulphonylmorpholine (*ca.* 35% on the morpholine content of the complex), m. p. 146—147°, undepressed by mixture with an authentic sample. In another experiment a small quantity of alcohol-insoluble material (m. p. >250°; equiv., 55; apparently ammonium chloride) was isolated.

The addition complex (6·3 mmoles) was added to ice-water (20 ml.) and zinc dust (10 g.). Acetic acid (10 ml. of 50%) was added portionwise, with shaking and cooling in ice. After 1½ hours the mixture was warmed on the water-bath for 25 minutes, basified, and steam-distilled. The distillate contained 3·3 milliequivs. of base, and the crude hydrochlorides obtained on evaporation yielded 4-toluene-*p*-sulphonylmorpholine (14% on morpholine content of complex).

THE UNIVERSITY, SHEFFIELD, 10. [*Received, July 19th*, 1952.]

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880. *An Improved Synthesis of Pyridine-2-aldehyde.*

By E. P. HART.

PYRIDINE-2-ALDEHYDE has been prepared in moderate or poor yield by several methods (see Dyson and Hammick, *J.*, 1939, 781; Kaufmann and Vallette, *Ber.*, 1912, **45**, 1736; 1913, **46**, 49; Niemann *et al.*, *J. Amer. Chem. Soc.*, 1942, **64**, 1678). Although Harries and Lénárt's method (*Annalen*, 1915, **410**, 95) also gives a poor yield of impure product, we have modified it so as to obtain the aldehyde in better yield and quality.

Experimental.—A slow stream (5 c.c./min.) of ozonised oxygen (10% of ozone) was passed during 1 hour into 2-stilbazole (Harries and Lénárt, *loc. cit.*) (5 g.) in dry ethyl acetate (100 c.c.), cooled to between −15° and −20°. Decomposition of the ozonide was accomplished by addition of water (10 c.c.), zinc dust (0·5 g.), N/10-silver nitrate (1 c.c.), and quinol (0·05 g.). After being kept overnight, the mixture was extracted with 3·7% hydrochloric acid (2 × 20 c.c.), and the extract heated on the water-bath to complete removal of benzaldehyde. The pyridine-2-aldehyde, b. p. 69—70°/16 mm. (1·7 g., 57%), was isolated after addition of aqueous potassium hydroxide and extraction with ether. Its yield is diminished if the quantities used are more than double those given.

The author is indebted to Dr. E. Tittensor for his interest in this work.

THE TECHNICAL COLLEGE, NOTTINGHAM. [*Received, July 23rd*, 1952.]

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881. *The Preparation of Arylalkanesulphonic Acids.*

By C. A. Bunton and E. A. Halevi.

In the course of a kinetic investigation it was necessary to prepare the sodium salts of a number of arylalkanesulphonic acids. The accepted method of preparation by heating the appropriate arylalkyl halide with aqueous sodium sulphite (see, *e.g.*, Suter, "Organic Chemistry of Sulphur," Wiley, N.Y., 1944, p. 114) was satisfactory with the bromides but not with the corresponding chlorides. As the chlorides can usually be prepared easily by chloromethylation, the general method was modified so as to utilize the chloride. This is converted into the corresponding iodide by treatment with sodium iodide in acetone solution; the iodide, which need not be isolated, is then converted into the sulphonate, in good yield, by warming it with sodium sulphite in aqueous acetone.

The simplicity and rapidity of this procedure, as well as its apparent generality, prompt us to report it.

Experimental.—The preparation of two typical sulphonates is described, one with, and the other without, prior isolation of the intermediate iodide.

Repeated microanalyses of these sodium sulphonates, as well as others prepared by the older method, yielded unsatisfactory and inconsistent results for carbon and hydrogen. They were therefore characterised as the *S*-benzylthiuronium derivatives (Chambers and Watt, *J. Org. Chem.*, 1941, **6**, 376).

(I) (a) *5-Methoxy-2-methylbenzyl iodide.* A solution of 2-methoxy-5-methylbenzyl chloride (17 g., 0·10 mole) (Ducasse, *Bull. Soc. chim.*, 1935, **2**, 1283; Quelet, *Compt. rend.*, 1934, **198**, 102) and sodium iodide (16·5 g., 0·11 mole) in acetone (100 c.c.) is warmed gently on a steam-bath for 15 minutes, and allowed to cool. The mixture is filtered, and the retained sodium chloride washed with a further 50 c.c. of acetone. The combined acetone solutions are poured on ice, and the *5-methoxy-2-methylbenzyl iodide* purified by recrystallisation from light petroleum as a pale yellow crystalline powder, m. p. 45—46°, decomp. on storage. An air-dried, freshly prepared sample was analysed (Found: I′, 47·9, 48·0. $C_9H_{11}OI$ requires I′, 48·4%).

(b) *Sodium 5-methoxy-2-methyltoluene-ω-sulphonate.*—The bulk of the uncrystallised iodide is redissolved in acetone (100 c.c.), and a solution of 27·5 g. (0·11 mole) of sodium sulphite ($Na_2SO_3,7H_2O$) in 100 c.c. of water added. The mixture is refluxed for 15 minutes, and the acetone boiled off. The hot aqueous solution is filtered, and the product allowed to crystallise slowly. The crystals are collected, and washed once with 10 c.c. of cold water and several times with alcohol. The *sodium* salt was further recrystallised from water and dried at 110° (Found: Na, 9·7. $C_9H_{11}O_4SNa$ requires Na, 9·7%). The *S-benzylthiuronium* derivative melted at 164° (Found: C, 53·6; H, 6·3; N, 7·4. $C_{17}H_{22}O_4N_2S_2$ requires C, 53·4; H, 6·0; N, 7·3%).

(II) *Sodium* iso*durene-α²-sulphonate* (*mesitylmethanesulphonate*). α²-Chloroisodurene (17 g., 0·10 mole) (*Org. Synth.*, 1945, **25**, 65) is treated with sodium iodide in acetone as in (I) (a). The iodide is not isolated but, after removal of the sodium chloride by filtration, is converted directly into *sodium mesitylmethanesulphonate* by warm aqueous sodium sulphite as in (I) (b) (Found: Na, 9·9. $C_{10}H_{13}O_3SNa$ requires Na, 9·7%). The *benzylthiuronium* derivative melted at 151° (Found: C, 55·3; H, 6·1; N, 7·4. $C_{18}H_{24}O_3N_2S_2$ requires C, 55·7; H, 6·1; N, 7·6%).

The yield is approximately 60%, based on the arylalkyl chloride. No attempt was made to improve the yield by working up the mother-liquors.

The authors are indebted to Professor E. D. Hughes, F.R.S., for his interest, and to the Humanitarian Trust and the Friends of the Hebrew University of Jerusalem for a maintenance grant to one of them (E. A. H.).

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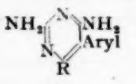
882. 3 : 5-*Diamino*-1-*aryl*-1 : 2 : 4-*triazoles as Potential Antimalarials.*

By (Miss) J. P. Thurston and James Walker.

The discovery of outstanding antimalarial activity in 2 : 4-diamino-5-arylpyrimidines (I; R = H or alkyl) (Falco, Goodwin, Hitchings, Rollo, and Russell, *Brit. J. Pharmacol.*, 1951, **6**, 185; Chase, Thurston, and Walker, *J.*, 1951, 3439) and the announcement that the active metabolite of proguanil (II) is 4 : 6-diamino-1-*p*-chlorophenyl-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine (III) (Carrington, Crowther, Davey, Levi, and Rose, *Nature*, 1951, **168**, 1080) suggested that noteworthy antimalarial activity might be found in other series of compounds containing the same common fragment $-N{:}C(NH_2){\cdot}N{:}C(NH_2){\cdot}X(Aryl)-$ (IV; X = C or N), an expectation which is borne out in the *as*-triazine series (V) (cf. Hitchings, Maggiolo, Russell, VanderWerff, and Rollo, *J. Amer. Chem. Soc.*, 1952, **74**, 3201).

We have examined a series of 3 : 5-diamino-1-aryl-1 : 2 : 4-triazoles (1-arylguanazoles) (VI), in which the six-membered hetero-ring of (I) and (III) has been replaced by a five-membered ring and in which the apparently significant grouping (IV; X = N) is included. None of these (VI; R = Ph, *p*-chlorophenyl, 2 : 4-dichlorophenyl, or 3 : 4-dichlorophenyl) showed detectable activity against *Plasmodium berghei* in the mouse at dosage levels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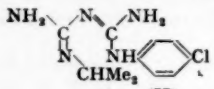
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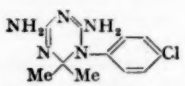
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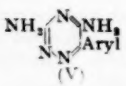
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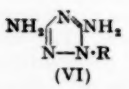
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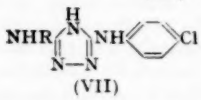
(VII)

greatly in excess of the levels at which (I), (II), and (III) are fully active; (VI; R = *p*-chlorophenyl) was also inactive against *P. gallinaceum* in the chick. The compounds (VI) were prepared by reaction between the appropriate arylhydrazines and dicyandiamide following generally Cohn's method (*J. pr. Chem.*, 1911, **84**, 409). As far as we are aware, the only other substance of this type which has been examined is (VI; R = *p*-bromophenyl), which has recently been found to be inactive (Hitchings *et al.*, *loc. cit.*), while the related series of 3-alkylamino-5-*p*-chloroanilino-1 : 2 : 4-triazoles (VII) also appears to be devoid of antimalarial activity (Curd, Davey, Richardson, and Ashworth, *J.*, 1949, 1739).

Experimental

3 : 5-*Diamino*-1-*phenyl*-1 : 2 : 4-*triazole* (VI; R = Ph).—A mixture of phenylhydrazine hydrochloride (14·4 g.), dicyandiamide (8·4 g.), and water (30 c.c.) was boiled under reflux for 2 hours, then cooled, treated with charcoal, and basified with a slight excess of 2N-sodium hydroxide, whereupon the pure product separated in colourless needles (11·4 g., 65%). It was recrystallised from ethanol and had m. p. 174—175°, as recorded by Pellizzari (*Gazzetta*, 1891, **21**, ii, 146).

The following 3 : 5-*diamino*-1-*aryl*-1 : 2 : 4-*triazoles*, all of which separated from alcohol in prisms, were prepared in an analogous manner from the appropriate arylhydrazines: 1-*p*-*chlorophenyl*- (yield 93%), m. p. 198—199° (Found: C, 45·4; H, 4·1; N, 33·5. $C_8H_8N_5Cl$ requires C, 45·7; H, 3·8; N, 33·4%); 1-(2 : 4-*dichlorophenyl*)- (yield 75%), m. p. 182—184° (Found: C, 39·1; H, 2·9; N, 28·2. $C_8H_7N_5Cl_2$ requires C, 39·3; H, 2·9; N, 28·7%); 1-(3 : 4-*dichlorophenyl*)- (yield 95%), m. p. 204—205° (Found: C, 39·0; H, 3·1; N, 28·7%).

Biological tests were carried out in the manner previously described (Chase, Thurston, and Walker, *loc. cit.*).

The authors are indebted to Miss M. M. Cameron and Mr. R. J. Clark for technical assistance.

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883. *The Vapour Pressure of Aqueous Solutions of Beryllium Sulphate and of Uranyl Sulphate at 25°.*

By R. A. Robinson.

The osmotic and activity coefficients of three uranyl salts have been measured recently (Robinson and Lim, *J.*, 1951, 1840). Measurements have also been made on uranyl sulphate (Secoy, *J. Amer. Chem. Soc.*, 1948, **70**, 3450) which indicate that this sulphate is anomalous at more than 1 *m*-concentrations, its activity coefficient being considerably higher than that of magnesium, zinc, or cadmium sulphate. This conclusion is derived from freezing-point measurements which yield activity coefficients at temperatures which decrease as the concentration increases. Thus an activity coefficient of 0·274 for uranyl sulphate at 3·5*m* and about −30° is compared with a value of 0·048 for zinc sulphate at the same concentration but at 25°. The heat-content and heat-capacity data necessary to correct over this temperature range are not available and Secoy could, therefore, do no more than draw attention to this anomaly. It is possible, however, that the anomaly results from a comparison of activity coefficients at very different temperatures rather than any peculiarity in the behaviour of uranyl sulphate. I have, therefore, measured vapour pressures of aqueous solution of this salt at 25° for direct comparison with those of other bivalent sulphates.

"AnalaR" beryllium sulphate has become available and the vapour pressures of solutions of this salt have been measured for comparison with those of magnesium sulphate (Robinson and Jones, *ibid.*, 1936, **58**, 959).

"AnalaR" $BeSO_4.4H_2O$ was used without further purification (Found: SO_4, 54·14. Calc.: 54·23%). Uranyl sulphate was prepared by addition of a slight excess of uranium trioxide to sulphuric acid, analysis of the solution for both U and SO_4, and addition of the amount of sulphuric acid required to give the exact stoicheiometric ratio. The ratio was checked by a further analysis. Isopiestic vapour-pressure measurements were made, sodium chloride being used as reference salt, with the results given in Table 1. A comparatively large number

Table 1. *Molalities of isopiestic solutions of sodium chloride and beryllium sulphate or uranyl sulphate at 25°.*

$BeSO_4$	NaCl	$BeSO_4$	NaCl	$BeSO_4$	NaCl	$BeSO_4$	NaCl	$BeSO_4$	NaCl
0·1022	0·06323	0·5671	0·3298	1·128	0·7268	2·205	1·824	3·135	3·147
0·1224	0·07510	0·5760	0·3362	1·272	0·8458	2·457	2·146	3·229	3·298
0·1304	0·8004	0·6621	0·3922	1·280	0·8531	2·497	2·206	3·429	3·615
0·2145	0·1287	0·6994	0·4162	1·499	1·051	2·589	2·328	3·506	3·750
0·3137	0·1844	0·7018	0·4174	1·674	1·228	2·678	2·456	3·898	4·406
0·3710	0·2157	0·8275	0·5011	1·888	1·508	3·039	2·995	4·086	4·730
0·4462	0·2615	0·8944	0·5485	2·177	1·791	3·064	3·041	4·286	5·082
0·5342	0·3091	0·9591	0·5988	2·194	1·808				
$UO_2{\cdot}SO_4$	NaCl	$UO_2{\cdot}SO_4$	NaCl	$UO_2{\cdot}SO_4$	NaCl	$UO_2{\cdot}SO_4$	NaCl	$UO_2{\cdot}SO_4$	NaCl
0·1132	0·06292	0·4570	0·2284	1·086	0·5895	2·386	1·705	4·605	4·226
0·1560	0·08389	0·5796	0·2917	1·251	0·7066	2·499	1·824	4·652	4·269
0·2265	0·1184	0·6542	0·3323	1·260	0·7129	2·776	2·117	5·317	5·022
0·2473	0·1257	0·6648	0·3364	1·346	0·7756	3·370	2·786	5·392	5·111
0·3261	0·1623	0·7405	0·3806	1·593	0·9711	3·373	2·786	5·983	5·726
0·3429	0·1703	0·8799	0·4630	1·789	1·137	3·466	2·893	6·069	5·806
0·3724	0·1849	1·063	0·5776	2·036	1·363	3·986	3·506	6·371	6·122

of measurements had to be made because it is not easy to plot the isopiestic ratio ($R = m_{NaCl}/m_{BSO_4}$) against m_{BSO_4}. Moreover, the values in the region of 0·1*m* are not of high accuracy because the concentrations of the reference salt, of the order of 0·05*m*, are not favourable to isopiestic measurements.

Since we know little about the activity coefficients of bivalent metal sulphates at concentrations below 0·1*m*, all activity coefficients have been calculated relative to an arbitrary

value of 0·150 at 0·1*m*. The values of the osmotic and activity coefficients at round concentrations are given in Table 2.

Beryllium sulphate behaves as might be expected: its activity coefficient is somewhat greater than that of magnesium sulphate as is consistent with the greater degree of hydration to be expected from the small radius of the beryllium ion (0·31 Å) in contrast to that of the magnesium ion (0·65 Å). Ion-pair formation must occur with both sulphates but should be less for beryllium sulphate because of hydration.

There is nothing about uranyl sulphate to distinguish it from other bivalent metal sulphates. To illustrate this, Table 2 includes values of the activity coefficient of man-

TABLE 2. *Osmotic and activity coefficients of beryllium sulphate and uranyl sulphate at 25°.*

	$BeSO_4$		$UO_2{\cdot}SO_4$			$MnSO_4$
m	ϕ	γ	ϕ	γ	γ (Secoy)	γ
0·1	0·582	(0·150)	0·529	(0·150)	(0·150)	(0·150)
0·2	0·560	0·109	0·488	0·102	0·108	0·106
0·3	0·544	0·0885	0·463	0·0807	0·080	0·085
0·5	0·535	0·0692	0·462	0·0611	0·056	0·064
0·7	0·548	0·0600	0·470	0·0515	0·049	0·053
1·0	0·580	0·0530	0·495	0·0439	0·047	0·044
1·5	0·658	0·0491	0·557	0·0385	0·053	0·038
2·0	0·757	0·0497	0·628	0·0367	0·066	0·035
2·5	0·889	0·0538	0·710	0·0370	0·090	0·035
3·0	1·019	0·0613	0·792	0·0383	0·131	0·038
3·5	1·171	0·0724	0·873	0·0401	0·274	0·042
4·0	1·327	0·0875	0·951	0·0433	—	0·048
4·5	—	—	1·025	0·0465	—	—
5·0	—	—	1·092	0·0500	—	—
5·5	—	—	1·150	0·0536	—	—
6·0	—	—	1·198	0·0571	—	—

ganese sulphate (Robinson and Stokes, *Trans. Faraday Soc.*, 1949, **45**, 612) which are of the same order as those of uranyl sulphate. Secoy's values for uranyl sulphate, also included, are in fair agreement with mine up to 1*m* but diverge considerably at higher concentrations and are of a different order of magnitude at 3·5*m*. This is not surprising because it is at these high concentrations that the correction to a uniform temperature is important. As a result of these experiments, I conclude that, although bivalent metal sulphates are undoubtedly complicated in behaviour, uranyl sulphate is no different from the others.

I am indebted to the Research Fund of the Chemical Society for assistance in this work.

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884. *The Preparation of Alkylarylarsines.*

By FREDERICK G. MANN and BRYAN B. SMITH.

CRAGOE, ANDRES, COLES, ELPERN, MORGAN, and HAMILTON (*J. Amer. Chem. Soc.*, 1947, **69**, 925) prepared methylphenylarsine by converting phenyldichloroarsine by the Meyer reaction into methylphenylarsinic acid, followed by reduction to the arsine, which is apparently the only alkylarylarsine hitherto recorded. For the preparation of a series of such arsines, it is advantageous to reduce phenylarsonic acid to phenylarsine and convert the latter in liquid ammonia into the monosodium derivative, PhAsNaH, which reacts readily with alkyl halides to give the alkylphenylarsine: only one reduction is thus required.

Experimental.—Liquid ammonia (200 c.c.) was placed in a flask fitted with a 3-necked adaptor carrying a mercury-sealed stirrer, a dropping funnel, and an exit tube packed with

cotton wool to prevent inward diffusion of air. Sodium (1·8 g., 1·1 mols.), cut into small pieces, was dissolved in the stirred ammonia, and phenylarsine (8 c.c., 1 mol.) in dry ether was then added dropwise, the blue colour of the solution changing to golden-yellow when the addition was complete. The alkyl bromide (1·1 mols.) was then slowly added, and after a few minutes' stirring the solution became colourless. The ammonia was allowed to evaporate, and all the volatile residue was distilled off at 14 mm. without fractionation. The distillate was then carefully fractionated in nitrogen under reduced pressure. The following arsines were colourless liquids which underwent rapid oxidation on exposure to air: *Ethylphenylarsine* (31% yield), b. p. 86·5—87·5°/14 mm. (Found: C, 52·65; H, 5·85. $C_8H_{11}As$ requires C, 52·75; H, 6·1%). *Phenyl*-n-*propylarsine* (51% yield), b. p. 96—97°/12 mm. (Found: C, 55·5; H, 6·8. $C_9H_{13}As$ requires C, 55·1; H, 6·7%). n-*Butylphenylarsine* (68% yield), b. p. 117°/15·5 mm. (Found: C, 57·0; H, 7·1. $C_{10}H_{15}As$ requires C, 57·15; H, 7·2%). The progressive rise in yield throughout this series is probably partly due to the decreasing volatility of the alkyl bromides; a portion of the ethyl bromide in particular may have been swept out of the apparatus by the stream of ammonia gas. Furthermore, these yields could doubtlessly be increased by working on a larger scale.

It is probable that these arsines in liquid ammonia solution will react with a second equivalent of sodium. When the quantities of sodium and of ethyl bromide in the above experiment were doubled, distillation gave diethylphenylarsine, b. p. 100·5—101°/11 mm., in 34% yield: it was identified by combination with cold methyl iodide, followed by conversion into diethylmethylphenylarsonium picrate, m. p. 85—86° unchanged by admixture with an authentic sample (cf. Beeby and Mann, *J.*, 1951, 890).

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885. *Quinaldinoyl Chloride.*

By D. LL. HAMMICK and A. M. ROE.

A SUBSTANCE described as quinaldinoyl chloride was first prepared by Meyer (*Monatsh.*, 1904, **25**, 1199; *Ber.*, 1905, **38**, 2488) by the action of thionyl chloride on quinaldinic acid. He described it as a very sparingly soluble, crystalline substance of m. p. 175—176°. Besthorn and Ibele (*Ber.*, 1905, **38**, 2127) claimed to have obtained, by the same reaction, an acid chloride of m. p. 96°, readily soluble in organic solvents. Meyer's inability to obtain Besthorn's product was ascribed by Besthorn (*Ber.*, 1908, **41**, 2003) to the presence of anticatalysts (notably tin) in the thionyl chloride used. It was suggested, in a long and inconclusive controversy summarised by Meyer and Turnau (*Ber.*, 1909, **42**, 1163), that the high-melting compound was a polymeric form of quinaldinoyl chloride.

Preparation of the lower-melting chloride was not recorded again until Hammick and Dickinson (*J.*, 1929, 214) made it by the action of phosphorus pentachloride on pure dry quinaldinic acid in ligroin (cf. also Krollpfeiffer and Schneider, *Annalen*, 1937, **530**, 34). However, the preparation requires not only absolutely dry quinaldinic acid, but also freshly distilled ligroin dried over sodium.

Spath and Spitzer (*Ber.*, 1926, **59**, 1480) suggested that the substance, m. p. 175—176°, might be the hydrochloride of quinaldinic acid. In the present note we adduce evidence that confirms this.

First, analyses agree with this requirement (Found: C, 57·3, 56·7; H, 3·8, 4·0; N, 6·7, 7·0; Cl, 16·9, 17·1. Calc. for $C_{10}H_8O_2NCl$: C, 57·2; H, 4·3; N, 6·45; Cl, 16·7. Calc. for $C_{10}H_6ONCl$: C, 62·7; H, 3·1; N, 7·3; Cl, 18·55%). Secondly, crystallisation from dry *cyclo*hexanone gave fine needles, m. p. 153° (decomp.), undepressed on admixture with quinaldinic acid. Thirdly, a specimen of quinaldinic acid hydrochloride, m. p. 177·5—181° (decomp.), prepared by crystallisation of quinaldinic acid from hydrochloric acid (25%), gave a mixed m. p. of 179—179·5° with the high-melting "chloride" (owing to the decomposition, no very firm conclusions can be drawn from these figures).

The infra-red absorption peaks for quinaldinic acid and the low- and the high-melting chloride (taken in a paraffin paste) leave the matter in no doubt (see Table). They

show that quinaldinic acid exists as a zwitterion in the solid state; this is confirmed by Flett (*J.*, 1951, 962), and provides a useful confirmation of the fact that this acid can be decarboxylated in polar solvents as the zwitterion (Brown and Hammick, *J.*, 1949, 659).

Compound	Max. (μ)			
Quinaldinic acid	—	5·18 medium, broad	—	
High-melting " chloride " (hydrochloride)	3·08 medium	5·05 strong, broad	5·82 strong	
Low-melting acid chloride	—	5·05 weak, broad	5·70 strong	5·82 weak

The absorption of the high-melting form indicates the presence of a hydroxyl (3·08 μ) and a carbonyl bond (5·82 μ). The genuine acid chloride shows no hydroxyl and has a carbonyl absorption at 5·70 μ as expected; it shows to a small degree the absorption of the high-melting material, and analysis of the same sample showed that partial hydrolysis had indeed occurred. The broad absorption shown by the above quinaldinium compounds near 5·1 μ, may be associated with the structure $-\overset{+}{N}H{:}C<$ (cf. Randall, Fowler, Fuson, and Dangle, " Infra-red Determination of Organic Structures," Van Norstrand, New York, 1949, for amino-acids and amino-acid hydrochlorides).

We record also that we have isolated, from the residue obtained after refluxing pure quinaldinic acid with phosphorus pentachloride in ligroin, the hydrochloride of Besthorn's Red (Krollpfeiffer and Schneider, *loc. cit.*). Work on this and analogous compounds will be reported later.

We thank Dr. F. B. Strauss for measuring the infra-red absorptions and for helpful discussions.

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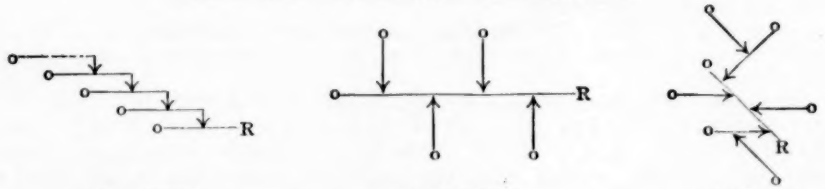
886. *Evidence of Multiple Branching in Waxy Maize Starch.*

BY STANLEY PEAT, W. J. WHELAN, and GWEN J. THOMAS.

THREE structural formulæ have been suggested for amylopectin, *viz.*, the Haworth laminated formula, Fig. 1*a* (Haworth, Hirst, and Isherwood, *J.*, 1937, 577), the Staudinger " comb " formula, Fig. 1*b* (Staudinger and Husemann, *Annalen*, 1937, **527**, 195), and the Meyer arborescent formula, Fig. 1*c* (Meyer and Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 865). Hitherto little experimental evidence has been forthcoming to distinguish between the three methods of branching since each appeared adequately to explain the known facts.

FIG. 1. *Possible structural formulæ for amylopectin.*



(*a*) Haworth. (*b*) Staudinger. (*c*) Meyer.

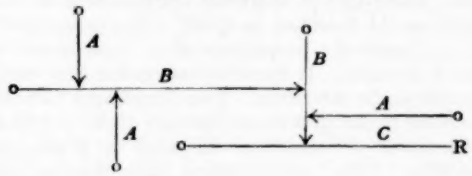
o = Non-reducing chain end, ↓ = α-1 : 6-Link, R = Free reducing chain end.

The essential differences may be expressed in the following terms. The Haworth formula represents a series of short linear chains (containing an average of 25 glucose units joined by α-1 : 4-links) mutually connected by α-1 : 6-glucosidic branch linkages in which the

average position of the branch link is at the centre of the repeating chains. This laminated formula implies a system of single branching and it differs from Meyer's formula in that the latter envisages multiple and random branching of the chains (Fig. 1*c*). The Staudinger and Haworth formulæ represent extremes, inasmuch as in the former all the branch links are carried by a single main chain.

It will be observed that three arrangements of the basal (linear) chains are possible; these are represented by chains *A*, *B*, and *C* in Fig. 2. The interlinking of a chain with one

FIG. 2. *Types of chains in amylopectin.*



or more other chains involves the reducing group ($C_{(1)}$) and/or primary hydroxyl groups ($C_{(6)}$) of the constituent glucose members. In a type *A* chain only the $C_{(1)}$ group is engaged and in a type *C*, only $C_{(6)}$ groups. The attachment of a type *B* chain is however effected through its $C_{(1)}$ group and also through one or more of its $C_{(6)}$ groups. In each amylopectin molecule there will be only one chain of the third type, *C*, since this carries the sole reducing end group. Each structure given in Fig. 1 contains one *C* chain but they are distinguishable in respect of the proportions of *A* and *B* chains. In the Haworth formula there is only one *A* chain per molecule whereas the Meyer formulation requires many *A*, as well as *B*, chains. The Staudinger structure contains, in addition to the *C* chain, only *A* chains; it contains no *B* chains. It follows that if the proportion of *A* chains in the amylopectin structure could be determined, a distinction between these rival formulations becomes possible. A method for the detection of *A* chains has now been developed from our enzymic studies.

Waxy maize starch (amylopectin) was hydrolysed to the limit with dilute crystalline β-amylase, maltose was removed by dialysis, and the limit β-dextrin isolated. This dextrin (4·19 g.) was treated with the debranching R-enzyme (Hobson, Whelan, and Peat, *J.*, 1951, 1451). The dialysable portion of the product (1·77 g.) was fractionated on a charcoal–Celite column (Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677; Bailey, Whelan, and Peat, *J.*, 1950, 3692). Glucose was not detected but maltose (0·278 g.; $0{\cdot}813 \times 10^{-3}$ mole) and maltotriose (0·282 g.; $0{\cdot}563 \times 10^{-3}$ mole) were obtained. The next product in order of increasing molecular weight was maltohexaose and this was followed by a continuous series of higher dextrins; maltotetraose and maltopentaose were not formed. Our interpretation of these results is as follows. Chains of type *A* will give rise, after the successive actions of dilute β-amylase and R-enzyme, to maltose or maltotriose according to whether they originally contained even or odd numbers of glucose units. Some of the *A* chains may of course consist initially of only two or three glucose units. Since the 4- and the 5-unit maltodextrins are not found among the products of debranching of limit β-dextrin, the length of the *B* chains in the β-dextrin (and therefore in the amylopectin) cannot be less than six glucose units. In other words, the maltose and maltotriose isolated as products of debranching can have come only from the *A* chains and not from the *B* chains.

Maltose and maltotriose were liberated by R-enzyme from the β-dextrin in the molar ratio, 1·45 : 1, although it might have been expected that equimolar quantities of these sugars would result, since the chances of an *A* chain containing an even or an odd number of glucose units are presumably equal. The discrepancy is possibly due to the incomplete removal of maltose during the initial dialysis of the β-dextrin. If 1·9% of the maltose produced by β-amylase had remained in the β-dextrin this discrepancy would be explained. It should be noted that the maltotriose is a product only of the debranching action of R-enzyme; it is not liberated by β-amylase acting alone on amylopectin.

If the laminated formula (Fig. 1*a*), having a single *A* chain, represents the structure of amylopectin, then the β-dextrin derived from it would yield, when debranched by R-enzyme, equimolar amounts of maltose amd maltotriose, corresponding to an average of 2·5 glucose residues per molecule. The actual molecular size of waxy maize β-dextrin has not been determined but since the results of Potter and Hassid (*J. Amer. Chem. Soc.*, 1948, **70**, 3774) indicate a variation between 6000 and 37,000 glucose residues per molecule for a number of amylopectins of plant origin the lower limit of 6000 may be taken as a minimum value for waxy maize starch. Since β-amylase removes about 50% of the molecule as maltose, it may be further assumed that the degree of polymerisation of the β-dextrin is at least 3000. The molar percentage of maltose + maltotriose to be expected from the Haworth model β-dextrin would therefore be 0·083. The actual yield was however much greater, namely, 5·3%. Clearly the proportion of *A* type chains is far higher than is implied by the laminated formula. It must be concluded that *multiple* branching is an intrinsic part of the amylopectin structure. The Staudinger formulation (Fig. 1*b*) must also be incorrect, since all the chains in it except one are of the *A* type and calculation shows that the proportion of maltose + maltotriose liberated by R-enzyme from the β-dextrin would be of the order of 25%. (The basal repeating chain of waxy maize starch contains an average of 20 glucose units; Brown, Halsall, Hirst, and Jones, *J.*, 1948, 27.) Accordingly, the multiple and random branching of Meyer's model (Fig. 1*c*) is favoured, since it implies a submaximal proportion of *A* chains.

Attention is drawn to the fact that the α-1 : 6-glucosidic linkage terminating an *A* chain at its potential reducing end does not interfere with the normal course of β-amylolysis except that the ultimate maltose or maltotriose unit remaining after the action of β-amylase on amylopectin (Fig. 2) would be part of the β-dextrin molecule. It may be that the linked 3-unit chain so produced is further degraded with the liberation of maltose by the prolonged action of a concentrated solution of β-amylase, as is maltotriose (Bailey, Whelan, and Peat, *J.*, 1950, 3692). This possibility is being investigated. [Added in proof, Oct. 9th, 1952: See Larner and Cori, *Chem. Eng. News*, 1952, **30**, 1524.]

The authors thank Dr. T. J. Schoch for a gift of waxy maize starch and the Department of Scientific and Industrial Research for a maintenance grant to one of them (G. J. T.).

University College of North Wales, Bangor. [*Received, September 1st*, 1952.]

OBITUARY NOTICES.

WILLIAM JOSEPH ELFORD.

1900—1952.

WILLIAM JOSEPH ELFORD, who died in London on February 14th, was trained as a physical chemist and used this basic training to make a fundamental contribution to microbiology in the course of his life's work at the National Institute for Medical Research. Born at Malmesbury on January 4th, 1900, Elford early distinguished himself at the local secondary—now grammar—school and proceeded to Bristol University after a year of service with the Royal Engineers at the end of the First World War. At the University he obtained the B.Sc. degree with First Class Honours in Chemistry, and, at the same time, gained his colours at cricket, hockey, and tennis. He was elected President of the University Chemical Society and held the Colston Research Fellowship for two years. Continuing in Bristol, Elford carried out a notable piece of research for the degree of Ph.D. under the supervision of Professor J. W. McBain on equilibria underlying the soap-boiling process, and, in particular, his phase studies of the difficult binary and ternary systems potassium oleate, potassium chloride, and water have provided a model for subsequent work. Elford actually carried out many experiments on a semi-commercial scale in the soap factory, and it is a tribute to his personality that he got on extremely well both with his colleagues and with the factory people in this old and secretive industry. The antiquity of soap manufacture in Bristol is probably not well known but it may be noted that the industry there dates from the fourteenth century and the city was regarded by Fuller in his " Worthies of England " (1662), " as the staple place thereof where alone it " (*i.e.*, " gray sope ") " was anciently made." Professor McBain describes Elford's graduate work as " being distinguished by the combination of novel, elegant and optical techniques with strict physical chemical methods " and these characteristics were typical of his precise and orderly method of work throughout his life.

Elford came to the National Institute for Medical Research, then at Hampstead, in October 1925, primarily to work under the late J. E. Barnard at a time when research work on viruses was just beginning. During the next five or six years he brought to perfection his technique for ultrafiltration by demonstrating how uniform collodion membranes of accurately graded porosity could be produced and calibrated. These membranes, of an altogether different degree of accurate and uniform porosity from anything previously known in ultrafiltration, ranged in pore size from about 3 μ to 10 mμ or less, and were the first tools available for measuring the sizes of viruses. During the following decade, Elford collaborated with a number of biological colleagues in estimating the sizes of numerous viruses by graded ultrafiltration, and immeasurably accelerated progress in this difficult field by the data which these researches provided. The methods developed in the course of this work were fully summarised by Elford in an outstanding monograph which he contributed to Doerr and Hallauer's " Handbuch der Virusforschung " (1938), entitled " The sizes of viruses and bacteriophages, and methods for their determination," while a more accessible and condensed account of Elford's work in relation to ultrafiltration in general is to be found in the article by J. Douglass Ferry (*Chem. Reviews*, 1936, **18**, 373).

With the outbreak of war in 1939, Elford was drawn into researches on air-hygiene, having regard to the possible eventuality of defence against bacteriological warfare and the more directly pressing problem of the conditions obtaining in air-raid shelters. In this work his talent for careful and critical experimentation was ever obvious though it was not in keeping with his painstaking methods to come to hasty conclusions so often demanded by *ad hoc* problems. One rarely saw Elford ruffled and the nearest he ever came to showing anger was when he had convinced himself that a piece of work relating to his own fields of interest had been carried out in a slipshod manner. In 1942, he was found to be suffering from fairly severe hypertension and a poor prognosis was given. Nevertheless, having resigned himself to restriction of some of his physical activities, he was able, after a period, to resume reasonably normal work except when recurring hypertensive episodes demanded rest. In spite of uncertain health, Elford's work was not yet done and he made one further outstanding contribution to scientific knowledge, the full application of which has not yet been explored. Becoming interested in electron microscopy, he showed that the ghosts of laked fowl red cells formed suitable objects for study with this tool. Furthermore, a number of medically important viruses, including those of

influenza, were shown to be adsorbed on to these ghosts, just as they are on to the intact cells, and were then revealed by electron microscopy in some of the most beautiful and telling photographs yet obtained with this instrument.

Elford remained a bachelor and by nature he was shy and reserved. A charming manner and cheerful smile, however, made him easily approachable by all and sundry and one had no difficulty in getting to know his sterling qualities, while his assistance and advice were freely sought by many and just as freely given. He became a Fellow of this Society in 1926 and was elected a Fellow of the Royal Society in 1950.

JAMES WALKER.

GEORGE ARMAND ROBERT KON.*

1892—1951.

GEORGE KON came to British science from an unusual background. He was born in St. Petersburg on February 18th, 1892, the only child of his parents. His father was a cultured and talented member of an old Polish–Jewish family, an excellent mathematician and linguist, and the son of a portrait painter; his mother, Marie Fleuret, was French. His father was a banker in a responsible position, and the family was comfortably off. George was a delicate child and was brought up with great care and devotion by his mother and an old nurse. In the candid and penetrating autobiographical notes which he left, he remarks ruefully " It is clear that I was unnecessarily coddled and spoilt and this was to prove a handicap in later life."

He was educated privately by a succession of instructors : a French governess, two Polish tutors (one, Adolf Dygasinski, an author of some note, who gave him a love for natural history), and a German governess. When he was ten, the family moved to Tientsin in North China where his father had become manager of the Russo-Chinese Bank. He spent three happy years in China where his liking for natural history developed into a passion for butterfly collecting. He published two short notes in the *Entomologische Zeitschrift* between the ages of sixteen and seventeen.

In Tientsin he first came into contact with the people whose nationality he was to adopt and was taught English by a " worthy though hideous " lady, the daughter of a missionary. A later move was to Vladivostok, " magnificent country for shooting and ideal for butterfly collecting," and here the family made friends with Sir Robert Hodgson, then British vice-consul. The first turning point in Kon's life came when Hodgson persuaded his parents to send him to Cambridge. Accordingly, in 1909 he passed the Russian equivalent of Matriculation and, after some coaching in Greek at a rectory near Wisbech, he went up to Caius to read Medicine.

The choice of subject was his parents'; he himself wished to read Science. He " found Anatomy very dull and uphill work " but enjoyed Physiology. He failed his Second M.B. Examination but got a Second in Part I of the Natural Science Tripos in 1912. Apart from this and a rather solitary first term, Kon found life at Cambridge enjoyable. He made several good friends, played lawn-tennis and golf, and began to lose his interest in entomology and to discover one in motor-cycling. The family plans involved a business position in Russia, but on his return there he felt a stranger and decided to take up a scientific career in England. Accordingly, 1913 found him living in chambers in St. James's and attending classes in chemistry and chemical technology at the Imperial College of Science and Technology, where his fellow students included C. K. Ingold and (the late) S. Sugden.

Up to this time George Kon's career had been that of the only son of a wealthy cosmopolitan family and his scientific tastes had not crystallised. But in February a second decisive event occurred with the arrival at South Kensington of Jocelyn Thorpe, newly appointed Assistant Professor of Organic Chemistry. Kon attended his lectures " and there and then decided to become an Organic Chemist."

August 1914 found Kon in the Tyrol, but it was in a fast car and he managed to cross the Brenner before the declaration of war. He returned to England by circuitous routes and joined the team at the Imperial College engaged on the preparation of essential drugs. He worked with Miss F. M. G. Micklethwait, under whose care, he says, " I soon realised that my ideas of what work meant had to be overhauled." He was naturalised in 1916 and joined the Army as a Lieutenant in the Anti-gas Department. Among his duties were the supervision of a

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respirator factory and a liaison visit to the United States of America when they entered the war. He was mentioned in despatches in 1917, and left the army at the end of the war with the rank of Captain.

His father and mother escaped from Russia at the time of the revolution, with the loss of most of their fortune, and the reunited family set up house together in London. Later his parents moved to Paris. Kon rejoined Thorpe, worked hard with few distractions, and received his D.Sc. for a thesis, on which his examiner, W. H. Perkin junior, wrote "I approve of this publication, it is an excellent piece of work." He had now found his scientific feet and was appointed Thorpe's private research assistant in 1923 and lecturer at the Imperial College in 1925. His duties were confined to the teaching of experimental Organic Chemistry and to research supervision. The work prospered. Thorpe treated him with his habitual generosity and a long stream of important papers began to flow; these are reviewed later.

In 1926, Kon married Anne Pollock (née Watts). The marriage was dissolved in 1937. In 1930 Kon suffered financially in the Wall Street slump. These troubles were offset by his steady professional advancement and the increasing recognition of his scientific work. In 1934 he was appointed Assistant Professor at the Imperial College. He became a member of Council of the Chemical Society in 1931—32 and again in 1933—36, and served on numerous of their committees. He made admirable contributions to the *Annual Reports on the Progress of Chemistry* in 1932, 1933, and 1934. He was elected a Fellow of the Royal Society in 1943.

In 1942 he was appointed to the chair of Chemistry at the Chester Beatty Research Institute of the Royal Cancer Hospital. He had been at the Imperial College for nearly thirty years, with the break during the war. He had worked under two leading personalities of the chemical world in Thorpe and Heilbron (who succeeded Thorpe in 1938) and had kept himself largely in the background. Nevertheless his services to the College were of the greatest value in maintaining the high reputation of the Organic Chemistry school in the period between the wars. The list of his colleagues and contemporaries at South Kensington includes a formidable section of contemporary academic organic chemistry: Thorpe, Heilbron, M. A. Whiteley, Ingold, Farmer, Dickens, E. R. H. Jones, A. H. Cook, Hey, Shoppee, J. W. Baker, Rothstein, Rydon, Harper, Owen, Barton, C. E. Dent, and a large number who have made outstanding contributions in chemical industry.

He remained at the Chester Beatty Institute for the remainder of his life doing valuable work on carcinogenesis and mutagenesis. His death came very suddenly, and was a great shock to those close to him. On March 15th, 1951, an important meeting sponsored by the Chemical Society and other bodies was held in Manchester to discuss the Chemistry of Cell Division. After the introductory papers Kon opened the discussion. He referred, among other things, to the correlation between cytotoxic activity and the chemical reactivity of the nitrogen mustards. He ended on a hopeful note, saying that the structural chemical approach would certainly yield results of importance to the general problem of cancer. At the end of his speech he collapsed and died almost instantaneously from heart-failure. Few scientists can have died so immediately in action. He had had some heart trouble in the preceding months, but the suddenness of the end was sadly unexpected. He suffered from a cleft palate and public speaking placed a heavy strain on him.

George Kon was a man of remarkable gifts, and had a great range of interests outside science. An excellent linguist, he was also a connoisseur, particularly of English eighteenth century furniture and of good wine. He was wirily built and a natural athlete; a good tennis player and an enthusiastic and formidable golfer. He had a wonderful sense of rhythm which came out alike in his walk, in his games, in his chemical manipulation, and in his unusual gifts as a ballroom dancer.

With his natural elegance in manners and appearance and great personal charm, George Kon sometimes seemed to his more prosaic colleagues as a being from some other and gayer world. He became an Englishman not only by naturalisation but completely; he thought like one and joked like one. His kindliness, sincerity, and happy disposition endeared him to all those who knew him and the world indeed seems a greyer place now he is dead.

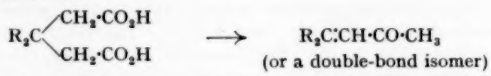
The last decade of his life was made happy by his marriage in 1938 to Mary Tress, who survives him.

Scientific work.

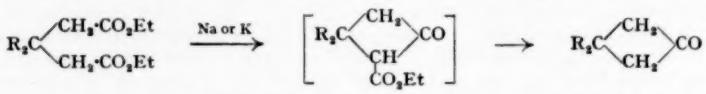
Kon's work was marked throughout by great care and quite unusual manipulative skill. He was a borne experimentalist, always happy to leave the desk for the laboratory bench. He was an expert glass-blower and a skilled analyst; almost to the end of his life he could be found

conducting his own micro-combustions. Several devices in technique and apparatus in common use today originated at his bench at the Imperial College. In interpretation and generalisation he was logical, cautious, and restrained. A good deal of his work involved repetition and re-evaluation of earlier material. The tone of his papers on controversial topics was always kindly and generous.

Kon's first research was carried out immediately after the end of the war of 1914—1919. It was a straightforward study of the neglected reaction of Guareschi, involving the condensation of cyanoacetic ester with ketones in the presence of ammonia. The results were published in a paper with Thorpe in 1919. Several important investigations followed on *spiro*-compounds. In 1921, Kon showed that the dry distillation of calcium salts of glutaric acids gave unsaturated ketones and not *cyclo*butanones :

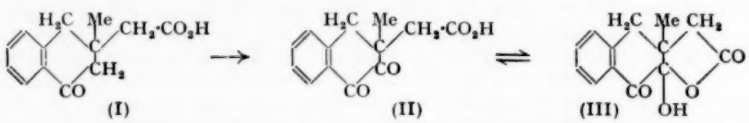


In the next year, Kon investigated the possibility of a cyclisation of the Dieckmann type on the corresponding glutaric esters. It was shown that the following reaction could occur :



These two papers were of great value in helping to reveal the limiting structural conditions for ring formation and formed the main part of Kon's thesis for the D.Sc. of London. Other aspects of the chemistry of ring formation and of the Guareschi reaction occupied Kon during this period. With S. F. Birch and Gough the bridging of Guareschi imides was studied, and it was shown that the bridged compounds could then be degraded to *cyclo*propane compounds such as caronic acid.

Concurrent work was being carried out in collaboration with another old Cambridge man working at South Kensington, Arnold Stevenson. This led to some surprising results. It was first found that cyclisation of the Guareschi product from benzyl methyl ketone yielded the tetrahydronaphthalene derivative (I). This substance was oxidised to the diketo-acid (II) which was found to give reactions of the isomeric hydroxy-lactone (III) :

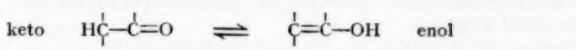


The various phenomena associated with these substances were explained on the basis of ring-chain tautomerism between (II) and (III).

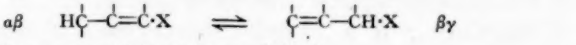
The fact that the reactions of this keto-acid could not be adequately explained on the basis of a single formula put Kon on the alert for other examples of chemical ambiguity. Almost immediately one came to hand. In 1912 Otto Wallach had obtained a ketone, $C_9H_{14}O$, by condensing *cyclo*hexanone with acetone. Kon had later obtained the same substance by heating calcium *cyclo*hexane-1 : 1-diacetate. The ketone has been given the structure (IV) with the

double bond $\beta\gamma$ to the functional group, mainly from the lack of exaltation in the molecular refractivity and of additive reactions with hydroxylamine and semicarbazide. On the other hand Norris and Thorpe in 1921 had found that the compound readily gave reactions characteristic of $\alpha\beta$-unsaturated ketones. Kon, Birch, and Norris accordingly re-investigated the compound. The previous ambiguous results were confirmed and amplified and it was shown that when the two distinct acid chlorides [corresponding in structure to (IV) and (V) but with Cl for CH_3] were treated with methylzinc iodide, the same ketone was obtained, which was identical with the Wallach–Kon product. The conclusion was that the two ketones were tautomeric under the conditions of formation and reaction.

These results were particularly important because they showed a practically unexplored territory and suggested the routes which exploration should take. At that time reversible isomeric changes were of course already well known, the best investigated being those of the keto-enol system :



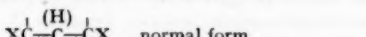
The formal tautomeric system of the Wallach–Kon ketone was of the three-carbon type :



(where X is the activating group which confers mobility).

A few other cases of reversible migration of double bonds in substituted propenes were known, notably some unsaturated αβ- and βγ-acids investigated by Fittig (X = CO_2^-) which isomerised in boiling alkali.

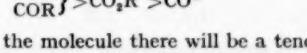
Wider recognition of three-carbon tautomerism had been delayed by the uncertainty over the nature of the aromatic bond. If benzene and other aromatic substances were examples of very mobile tautomeric systems which could not properly be represented by any one unsaturated structure, then it might seem reasonable to believe that among olefinic compounds some highly activated systems might be found which might have properties resembling the aromatic. There would of course be an essential difference that the aromatic systems could show no movement of an atom whereas in the propene system there would be a mobile hydrogen which would have to be accommodated somewhere in the formula. The term " semi-aromatic " had in fact been coined by Thorpe to describe the very mobile glutaconic acids, and the preferred state of the molecule was believed to be the " normal " form in which the hydrogen atom was left in an intermediate position between the α- and γ-carbons :



Kon might have followed this lead, particularly as the single Wallach ketone had appeared as the product of many different preparative methods. But from the first he avoided this mistake. The Wallach ketone was regarded as an ordinary equilibrium mixture of the two forms, which were too labile for isolation by the methods then available. The glutaconic acid group was put on one side for later study, and attention was immediately directed to other, less mobile, three-carbon systems. This strategy was fully vindicated. Two years later Kon and the writer discovered a pair of unsaturated ketones resembling the Wallach mixture (IV) and (V) but derived from diethyl ketone instead of *cyclo*hexanone. These two compounds could be isolated as definite individuals and their controlled inter-conversion studied. Three years after this, with Dickens and Hugh, Kon was able to isolate the two individual αβ- and βγ-forms of the Wallach ketone and to show that they readily passed into the already known equilibrium mixture. Finally, after a long study of the three-carbon system, Kon was able to turn to the glutaconic type and clarify the many puzzling features of its chemistry.

The main results of the work of Kon's school on three-carbon tautomerism are summarised below.

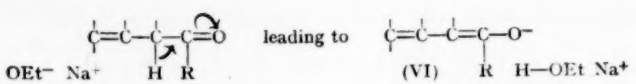
The movement of the double bond in an olefinic hydrocarbon usually only occurs under drastic experimental conditions. For tautomeric change to become important it is necessary for there to be present some unsaturated, electron-attracting *activating group*. The double bond can then migrate between the positions αβ and βγ to this group [as in formulæ (IV) and (V), for example]. So far as is known, double bonds in more remote positions behave like those in hydrocarbons and are comparatively non-mobile. Systems with two activating groups, αα′, αβ, or αγ are more mobile. The order of efficiency of the common activating groups is :



If only one such group is present in the molecule there will be a tendency for the double bond to conjugate with it, so that in the simplest possible case the migration will be virtually irreversible in the direction βγ ⟶ αβ :

For the change to become reversible, in the absence of a second unsaturated group, the βγ-form must be stabilised by alkyl substitution. This gives two products of sufficiently equal stability to undergo tautomeric change under suitable conditions.

The primary process in a typical three-carbon change is the labilisation of the mobile hydrogen. This is effected by a combination of internal weakening of the carbon–hydrogen bond by an electromeric process originating with the activating group, together with the external pull of an anion or anionoid molecule. Thus for the tautomerism of a βγ-ketone catalysed by sodium ethoxide the initial stage is :



The relative efficiencies of alkoxides as catalysts depend on the acidity of the corresponding alcohols; the more acid the alcohol (that is, the more stable the alkoxide ion) the less will be its tendency to remove hydrogen in the above process. Socium *iso*propoxide is therefore a good catalyst.

The analysis of a mixture of αβ- and βγ-isomerides is generally carried out by taking advantage of the comparative inactivity of the αβ-forms towards various halogen reagents which react readily with the βγ-isomerides. The composition of a tautomeric mixture is readily found by comparison with known mixtures. In this way the *position of equilibrium* can be found. It is normally independent of the method by which it is attained although small shifts have been observed in acid-catalysed systems. The *mobilities* of three-carbon systems can be compared by a kinetic study of the velocities of change under the same standardised experimental conditions.

When the hydrogen has been removed from a tautomeric ketone (or similar substance) the residual material, as pointed out by Ingold, can be represented as the enolic ion (VI). When the hydrogen returns to this it can give rise to either the αβ- or the βγ-unsaturated keto-form. The question arises how far this recombination occurs in the alkaline medium. If the enolate were stable in the presence of the alkaline catalyst, then recombination would take place largely or wholly on the final acidification of the alkoxide solution. There is, of course, no general answer to the question. Very weak acids such as carboxylate ions or monocarboxylic esters do not enolise appreciably so that at least the bulk of recombination takes place continuously during the equilibration. On the other hand, systems with two activating groups such as α-cyano-esters are comparatively acid, and fairly stable solid sodio-compounds can be isolated. When these are acidified two possibilities arise which are represented in a simplified form below :

The question arises whether it is possible to convert sodio-compounds into the βγ-tautomerides (process *b*) without invoking the more complex process (process *a*) by which the αβ form is produced. This point was carefully studied by Kon and his co-workers and it was shown conclusively that under the right experimental conditions the enol ⟶ βγ-unsaturated ketone change could in fact be carried out with little or no formation of the αβ-unsaturated keto-form, even when the latter was the more stable isomer of the three-carbon pair. The same technique was used in Kon's first paper on glutaconic acids in 1931, and in later work in the glutaconic series Kon, particularly with E. M. Watson, was to use this method with great success.

Quantitative investigations led to the establishment of certain regularities in the effect of substitution on the speed and direction of tautomeric change. Thus in unsaturated acid systems of the type :

$$R_2C{=}CH{\cdot}CH_2{\cdot}CO_2H \rightleftharpoons R_2CH{\cdot}CH{=}CH{\cdot}CO_2H$$

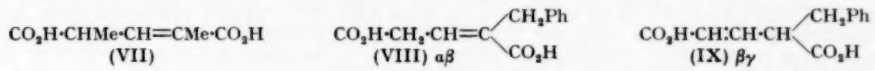
the proportion of βγ-form at equilibrium varies with R as follows :

R,R	H,H	Me,H	Et,H	Me,Me	Et,Me
Equilibrium, βγ, % ...	2	32	26	77	77

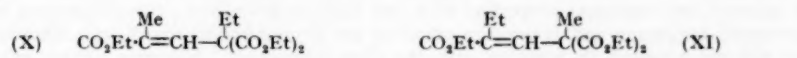
β-Alkyl groups have a similar but weaker effect, whereas an α-alkyl group stabilises the αβ-unsaturated form in acids. Unsaturated esters in general show the same results as the acids. Among unsaturated ketones β- and γ-alkyl groups give the expected stabilisation of the βγ-form but α-alkylation produces an unexpected shift in equilibrium in the same direction, that

is, it produces the opposite effect from that observed with acids and nearly all esters. There are also peculiar differences between the equilibrium data of various alicyclic systems, where the five-, six-, and seven-membered rings do not behave in a uniform manner. A considerable effort was devoted to the elucidation of the governing general rules, but the results do not lend themselves easily to summary.

By 1931, the main factors which influence double-bond migration in carbon chains were clear. Armed with this knowledge, Kon attacked the problem of glutaconic acids. The semi-aromatic formulation for the more stable forms of these substances had just received a heavy blow in the resolution at the Imperial College of " normal " αγ-dimethylglutaconic acid which accordingly had to be assigned the conventional formula (VII). Kon believed strongly that the chemistry of the glutaconic acids would have to be explicable on the basis of three-carbon tautomerism, complicated by *cis-trans*-isomerism. He used the techniques developed during the previous decade, particularly controlled regeneration from alkali derivatives and ozonolysis, coupled with careful determinations of physical constants and of halogen addition for the assessment of purity and double-bond position. The problem was rapidly solved along

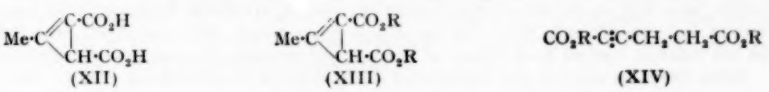


these lines, although the work brought out some unexpected features. For example, α-benzylglutaconic acid can theoretically exist in two structurally isomeric forms (VIII and IX), each with two geometrical modifications. Kon found that the two acids normally encountered differed not only in configuration but also in double-bond position, being in fact the *cis*-αβ- and *trans*-βγ-forms. The stabilities of the substituted glutaconic acids vary widely with the groups present and some of the possible structures were found to be incapable of isolation. An equivalence of the α- and the γ-position in the glutaconic acid system had been postulated by Thorpe. For example, the two tricarboxylic esters (X) and (XI) had been found to yield the same γ-ethyl-α-methylglutaconic acid on hydrolysis. Kon found that this and similar phenomena were due to the high mobility of the system which led to the formation of equilibrium mixtures.



Kon's general conclusions on the structure of the isomeric acids agreed broadly with the earlier views of Feist, although the latter tended to rely on purely stereochemical explanations of isomerism and did not fully appreciate the part played by double-bond migration.

While this strong evidence was accumulating that the glutaconic acids, although complicated, were conventional three-carbon systems, a difficult problem remained to be solved. Early work on 3-methyl*cyclo*prop-2-ene-1 : 2-dicarboxylic acid (XII) had led to the proposal that the acid had the " normal " or semi-aromatic structure and that it gave rise to three series of interconvertible esters, called normal, labile, and enol. Geometrical isomerism could not be invoked to explain the existence of three esters. Kon's re-examination showed that the " normal " ester had the Δ^2-structure (XIII) and that no other ester simply derived from the acid could be isolated. The " labile " ester could indeed be formed from the " normal " ester by the action

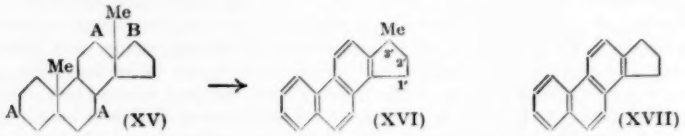


of heat but the process involved a remarkable and deep-seated change of the carbon skeleton, the product having the structure (XIV). Under the conditions believed to yield an enol ester, addition of alcohol to the double bond occurred. This careful investigation of Kon's showed that the acid and the ester (XII and XIII) did not exhibit the usual properties of three-carbon tautomers or, indeed, of glutaconic acids. The last necessity for the " normal " form thus disappeared and Kon, as he characteristically remarked, had " made honest compounds of the glutaconic acids."

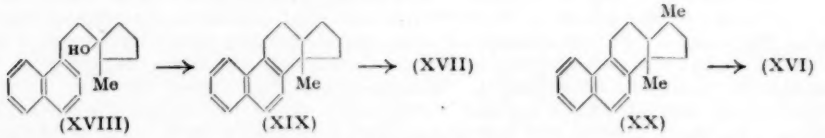
From these studies, Kon turned to a new field. The classical work of Wieland, and of Windaus, had begun to bring out of the mists the chemical nature of the steroids and bile acids. Structural formulæ for cholesterol and other key compounds were advanced. After some uncertainty the belief grew that the steroids were based on the tetracyclic structure (XV)

where A may be hydroxyl groups and B is a variable side chain. We may note that this structure has very recently been confirmed by several total syntheses.

In 1933 a key compound in the structural analysis was the " Diels hydrocarbon," $C_{18}H_{16}$. Diels had prepared this by the dehydrogenation of cholesterol and ergosterol. At first it was thought to be a hydrochrysene. Subsequently a structure based on *cyclo*pentenophenanthrene (XVII) was favoured. Elementary analysis did not permit a clear distinction between *cyclo*pentenophenanthrene itself (XVII), $C_{17}H_{14}$, and a monomethyl derivative, $C_{18}H_{16}$, such as (XVI). *cyclo*Pentenophenanthrene (XVII) was accordingly synthesised by Kon, and simultaneously and independently by L. Ruzicka and by J. W. Cook and their co-workers. The synthetic material was very similar to the Diels hydrocarbon but there were differences between the derivatives, and the crystallographic evidence of Bernal and Crowfoot finally showed that they were not the same. On the other hand the resemblances, particularly in absorption spectra, were so close as to encourage belief that they were nearly identical in structure. Kon accordingly, with S. H. Harper and F. C. J. Ruzicka, undertook the synthesis of the 3′-methyl compound (XVI). For this Kon used the following approach, typical of his care and good sense. 2-Methyl*cyclo*pentanone was found to react with the Grignard compound from 2-α-naphthylethyl bromide to yield the alcohol (XVIII). Cyclisation of this with phosphoric oxide gave a tetracyclic hydrocarbon which yielded *cyclo*pentenophenanthrene (XVII) on dehydrogenation, with elimination of the methyl group. Hence its structure must have been (XIX). The sequence of reactions was then repeated, 2 : 5-dimethyl*cyclo*pentanone being used



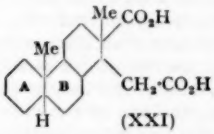
as starting material. The penultimate hydrocarbon was (XX) and its dehydrogenation gave 3′-methyl*cyclo*pentenophenanthrene (XVI). The synthetic compound was found to be identical in physical and chemical properties with the Diels hydrocarbon. Simultaneously and independently Bergmann and Hillemann prepared the 3′-methyl compound by a different process but did not establish its identity with the Diels compound. Rigorous further examination by Kon, and in the other laboratories concerned, showed that all three substances were the same. 3′-Methyl*cyclo*pentenophenanthrene was thus proved to be an important product of the dehydrogenation of cholesterol. This was a major piece of evidence in establishing the structure of the steroids on their present firm basis.



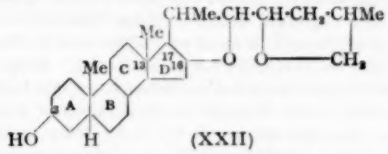
Although Kon was to publish several other papers on synthetic topics related to steroids they were of less importance than the successful coup which had just been described. In 1935—36 his interest turned to a group of the natural steroids themselves—the steroid sapogenins. From them he was led into the related sapogenins of the triterpene group. He worked on these two classes of sapogenins for 6—7 years.

Steroid sapogenins have recently been the subject of considerable study, partly because of the possibility of their conversion into the sex hormone, progesterone. At the time Kon began to work in the field there were several pieces of evidence connecting them in structure with the steroids. In particular, Tschesche had degraded tigogenin (from *Digitalis*) to *ætio*-5-*allo*-bilianic acid and thus connected it securely with the normal sterols of the cholestane series, in which rings A and B are fused in the *trans*-configuration. Kon carried out a similar degradation on sarsasapogenin acetate. The end-product was *ætio*bilianic acid (XXI) identical with a well-known breakdown product of the bile-acid group. From this result and from an earlier comparison of the behaviour of *Digitalis* and sarsaparilla sapogenins as surface films (with Askew and Farmer), Kon proposed the formula (XXII) for sarsasapogenin, making it into a geometrical isomeride of Tschesche's tigogenin.

During this work Kon isolated from Jamaica sarsaparilla root an isomeric genin which he called smilagenin. He subsequently connected this with sarsasapogenin in a manner which established that the difference between them lay in the configuration of the side-chain attached to $C_{(16)}$ and $C_{(17)}$. Recent work by Marker has led to a modification of the Tschesche formulation of the side-chain and the accepted partial formulæ for sarsasapogenin and smilagenin today are (XXII*a*) and (XXII*b*) respectively, the remainder of the molecule being as in (XXII). Kon's work established for the first time the existence of two typical kinds of isomerism of the



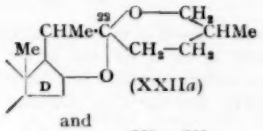
(XXI)



(XXII)

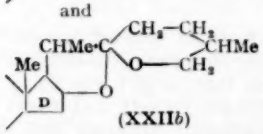
steroid sapogenins; namely that of the A/B ring fusion, and that in the side-chain at $C_{(22)}$. In later work, Kon with Woolman fixed the $C_{(3)}$ position of the hydroxyl group in sarsasapogenin. He also isolated a new sapogenin from the seed kernels of *Bulanites aegyptica*.

The more complex triterpene sapogenins next claimed his attention. These substances occur in various plant materials in the form of their glycosides, the saponins. They contain thirty carbon atoms and those of known structure have five alicyclic rings. They are closely related in structure to a number of other triterpenes which occur free in various plant resins, saps, and barks. With one or two exceptions the triterpene sapogenins of known structure are related to one triterpene, β-amyrin, the accepted formula for which, due to R. D. Haworth, is (XXIII). A distinguishing characteristic of these triterpenes is that on dehydrogenation they yield a mixture of aromatic compounds made up of sapotalene (1 : 2 : 7-trimethylnaphthalene), 1 : 8-dimethylpicene, and other materials.

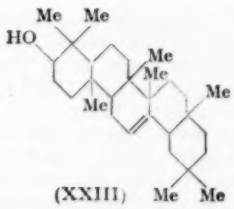


(XXII*a*)

and

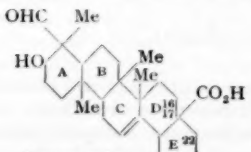


(XXII*b*)



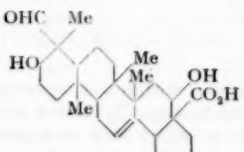
(XXIII)

Many plants belonging to the *Caryophyllaceae* contain rather large amounts of saponins. That from *Gypsophila* (soapwort) had been hydrolysed to the sapogenin, gypsogenin, and the structure of this had been shown by L. Ruzicka to be (XXIV). Its connection with two other sapogenins hederagenin and oleanolic acid had been established. Kon selected a second member of the order in fuller's herb (*Saponaria officinalis*). From the root of this a saponin was obtained which on hydrolysis yielded gypsogenin identical with that made by Ruzicka. Kon also reviewed Wedekind's examination of the sapogenin (" githagenin ") from corncockle and came to the conclusion that it also was identical with gypsogenin. He suggested that this genin may be characteristic of the *Caryophyllaceae*.

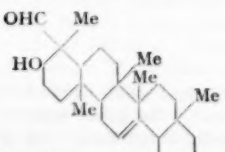


Gypsogenin

(XXIV)



(XXV*a*)



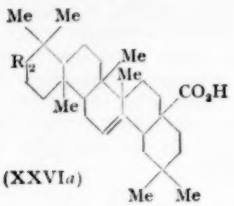
Quillaic acid

(XXV*b*)

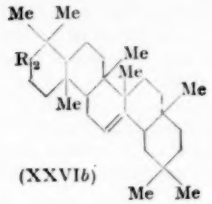
A compound of related structure is quillaic acid, on which Kon published several valuable papers. This is a fairly accessible triterpene as quillaia saponin (from soapbark) is used in commerce. A possible structure was shown to be that of a hydroxygypsogenin. Kon's

experimental results, which included measurements of the areas of unimolecular surface films, were first interpreted on the basis of a $C_{(16)}$-hydroxyl group, a *trans*-locking of rings D and E, and a $C_{(17)}$-carboxyl group (XXV*a*).

In later experiments the unimolecular film technique was applied to a number of other triterpene sapogenins containing acidic or ester functions. This involved studies of the conversion of oleanolic acid (XXVI*a* or *b*; R = OH) successively into the 2-keto-acid (oleanonic) and the deoxy-acid (γ-oleananic acid). The measured unimolecular film areas of these molecules differed from those expected on the basis of the Haworth formula. Kon was therefore led to propose that the carboxyl group in these triterpene acids was in a terminal ring. The $C_{(20)}$-position was selected as the most probable, which would lead to structure (XXVI*b*; R = OH) for oleanolic acid, and (XXV*b*) for quillaic acid. Later papers by Kon with Bilham and W. C. J. Ross produced further physical evidence in support of the $C_{(20)}$-position of the carboxyl group. For example, film measurements on derivatives of β-boswellic, ursolic, and betulic acids agreed with the view that the carboxyl, the only polar group, was at the end of the molecule. An examination of glycyrrhetic acid, the sapogenin of liquorice root, also led to results consistent with the new position for the carboxyl group. On the other hand the ready lactonisation of oleanolic acid observed by Ruzicka's school agreed better with the Haworth formula (XXVI*a*; R = H), and necessitated a modification of the formula proposed by Kon.



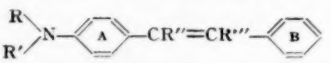
(XXVI*a*)



(XXVI*b*)

Although Kon's proposals were consistent and well argued it now appears that the surface film measurements do not provide a safe diagnostic method in this series. Recent work, particularly by Barton and E. R. H. Jones, provides strong support for the original Ruzicka–Haworth structures, of the type (XXVI*a*) and (XXV*b*), and the $C_{(17)}$-position of the carboxyl group is generally accepted today.

Kon's work in the sapogenin field ended in 1942, on his appointment to the Chair at the Chester Beatty Research Institute of the Royal Cancer Hospital. His introduction to chemical carcinogenesis came towards the close of a phase in that subject which had lasted for some fifteen years, and during which Kennaway, Cook, Hieger, Hewett, and others had established the importance of the polycyclic aromatic hydrocarbons. Although Kon had earlier been indirectly associated with these researches through his syntheses of *cyclo*pentenophenanthrene and Diels' hydrocarbon, his immediate contributions were at first limited to studies of various hydrocarbons and hydroxylated derivatives—*e.g.*, the isomeric propenylnaphthalenes, and the important metabolite 8-hydroxy-3 : 4-benzopyrene—in relation to the mechanism by which carcinogenic compounds are detoxified in the animal body. Soon, however, there arose a fresh and major development through the discovery of carcinogenic activity in 4-aminostilbene. Thereafter Kon played a leading part in an extended and fruitful investigation (with A. Haddow, R. J. C. Harris, and Edna M. F. Roe) whereby the main features of this structure (XXVII), *viz.*, the polar group, the ethylene bridge, and the nuclei A and B, were modified in such a way



(XXVII)

as to shed much light on the relations within this series of chemical constitution and biological action. The great majority of the biologically active compounds proved to be stilbenes with a basic substituent, the position of which was of paramount importance, *o*-dimethylaminostilbene, for example, being very much less active than the *p*-isomeride, and the *m*-compound completely inactive. Activity was further shown to depend on the integrity of the ethylene bridge, since it disappeared when either of the hydrogen atoms was substituted, when the bridge was reduced, when it was extended to contain three or more carbon atoms, when either methine group was replaced by a nitrogen atom, or when the bridge itself was absent or was replaced by oxygen or sulphur. Activity was also dependent on the *trans*-configuration of the molecule

about the ethylenic bond, and to a large extent on a free *p'*-position. These and other facts suggested the working hypothesis that one of the features required for activity was an unbroken conjugation of the amino-group with both nuclei, enabling the compound to assume some dipolar quinonoid character depending, among other things, on the co-planar arrangement of the two benzene nuclei which characterises the *trans*-form of the stilbenes. When evidence concerning steric conditions was compared with the biological activities of these compounds, a close parallel was suggested between lack of activity and buckling of the molecule. Thus in the inactive 4-dimethylaminostilbene derivatives with substituents on the α- and β-carbon atoms of the ethylenic double bond, or with methyl groups at two *ortho*-positions in a phenyl group, steric factors reduce the planarity of the molecule, so affecting the conjugation resonance characteristic of the molecule as a whole. All the evidence from diagrams, models, and spectra suggested that steric interference with the planar configuration in this series varies continuously from the planar 4-dimethylaminostilbene to the highly buckled αβ-diethyl derivative. Hence it appeared, in short, that biological activity within this series depends on a conjunction of such factors as molecular size and shape, and the apposition of a planar molecule to a hypothetical receptor surface. Kon obtained a great deal of satisfaction from this relatively complete study, and it is of interest that the foregoing conclusions have in general been supported by a more recent investigation by L. E. Sutton and others involving measurement of the electric dipole moments.

Kon next made an outstanding contribution to yet another development, with which he was still very actively concerned at the time of his death, namely, a study of the cytotoxic action of various new series of halogenoalkylarylamines (" aromatic nitrogen mustards ") and the discovery of their carcinogenic action. Although this investigation originated in an attempt to augment the cytotoxic and therapeutic action of the chloroethylamines, and especially to determine in what types of aromatic amine the *NN*-di-2-chloroethyl side-chain could still contribute its specific cytotoxic properties, it rapidly developed along unexpected lines to yield much fundamental information. It soon became obvious, as had been suspected by others for the aliphatic series, that cytotoxic activity depended on the presence in the molecule of two halogenoalkyl groups. It was this feature which led three of Kon's junior colleagues—namely, R. J. Goldacre from the general aspect of adsorption of drugs to protein, A. Loveless from the standpoint of chemical cytology, and W. C. J. Ross from a consideration of the kinetics of reaction of such two-armed compounds—to formulate what could be regarded as among the simpler possible explanations, that such substances might produce their cytotoxic effects in general, and various characteristic chromosomal and mitotic abnormalities in particular, through a process of cross-linkage between the constituent linear macromolecules of the chromosomes themselves. The new hypothesis soon led (partly owing to a suggestion from J. B. Speakman) to the synthesis by Kon and his colleagues of a series of diepoxides related to those previously employed as cross-linking agents in various textile applications, and to their subsequent biological test. These were the first of a number of chemical types all yielding the same carbonium ion, and at once it became evident that they were able to produce cytotoxic effects largely indistinguishable from those due to the di(halogenoalkyl)amines themselves; several, including the simplest of the series, namely 1 : 2-3 : 4-diepoxybutane, later proved to be carcinogenic as well. Although the cross-linking hypothesis is now known to represent an unduly simplified interpretation, and other possibilities are equally likely, it has in fact proved immensely fertile in development, and there can be no doubt of the significance for chemical carcinogenesis that these agents, and others discovered later, may operate by the biological alkylation of genetic protein. As can well be imagined, Kon took the greatest interest in these and related developments, and was ever ready to assist, whether by generous encouragement or a wise and kindly criticism. As has already been indicated, his death occurred immediately after he had opened the discussion at a meeting on " The Chemistry of Cell Division " held on March 15th, 1951, in Manchester. In his introduction Kon had stressed the satisfactory correlation between cytotoxic activity and the degree of purely chemical reactivity of the " nitrogen mustards " as measured by hydrolysis rates. On the question whether the effect of chain length could be attributed to steric or to polar factors, the answer seemed to him to be fairly clear, namely, that the two ends of the chain could be separated within limits, but that if the distance of the terminal carbon atom from the nitrogen atom was much increased beyond two carbon atoms, the activity fell off sharply, as did the rate of hydrolysis. If, however, this separation was achieved by inserting CH_2 groups between two nitrogen atoms so placed as to exert their polar effect and favour the production of a carbonium ion, the lengthening of the chain effected but little decrease in biological activity. Kon concluded that he had

every hope from all this work of eventual results with a very positive bearing on the cancer problem as a whole. Whether or not such will prove to be the case—and it is probable—his own contributions, together with those of his earlier career, ensure him a lasting and an honoured place not only in pure chemistry and the chemistry of natural products, but also in chemistry in its modern relation to biology and medicine.

In the preparation of this notice I have been greatly helped by Mrs. Mary Kon and by Professor A. Haddow. Professor Haddow very kindly reviewed the work done at the Chester Beatty Institute.

R. P. LINSTEAD.

J. R. PARK.

1902—1952.*

BRITISH applied science has suffered a severe loss in the untimely death, on July 30th, 1952, of Mr. J. R. Park, a Managing Director of the British Oxygen Company. Mr. Park was born in London in 1902 and was educated first at Battersea Grammar School and then at Queen Mary College where he graduated in chemistry. After a short period on the staff of Westminster Technical College he worked as an analytical chemist in industry for a number of years in Britain, and then for a year in a French firm.

In 1929 he joined Imperial Chemical Industries Limited, Billingham Division, where he remained until 1945. For a time he worked there as a plant manager, but soon he moved to the research side. The production of hydrogen, hydrogenation of coal, synthesis of ammonia, and synthesis of methanol were some of the fields which occupied him in the years up to the war; he had by then advanced to the position of Ammonia Research Manager. He was also connected with the design of oil hydrogenation plant and in the first year of the war was responsible for the design of various other plants. The writer made his acquaintance in 1941, when Park was put in charge of the Billingham research team working on the British Atomic Energy Project. His quick grasp of problems, his strong scientific background, and his understanding of large-scale industrial processes formed a combination that contributed greatly to the success of the enterprise.

In 1945 Park was asked to organise a research department in the British Oxygen Company. He did this with outstanding success, creating within a few years a large and flourishing research organisation practically from scratch. His worth was quickly appreciated; in 1948 he became Assistant Managing Director, and soon was promoted to the post of Managing Director. It is largely due to Park that the British Oxygen Company has been transformed from an undertaking relying mainly on foreign patents into a modern enterprise standing on its own feet in the field of research and development. Park was one of the all too small group of first-class British chemical technologists who are essential for the economic future of this country; his death leaves a gap which will be felt for a long time. His friends mourn the passing of a personality of wide interests and great charm, and of a warm-hearted and loyal companion.

Park became a Fellow of the Society in 1945 and was a member of the Finance and General Purposes Committee from 1948 to 1952.

F. E. SIMON.

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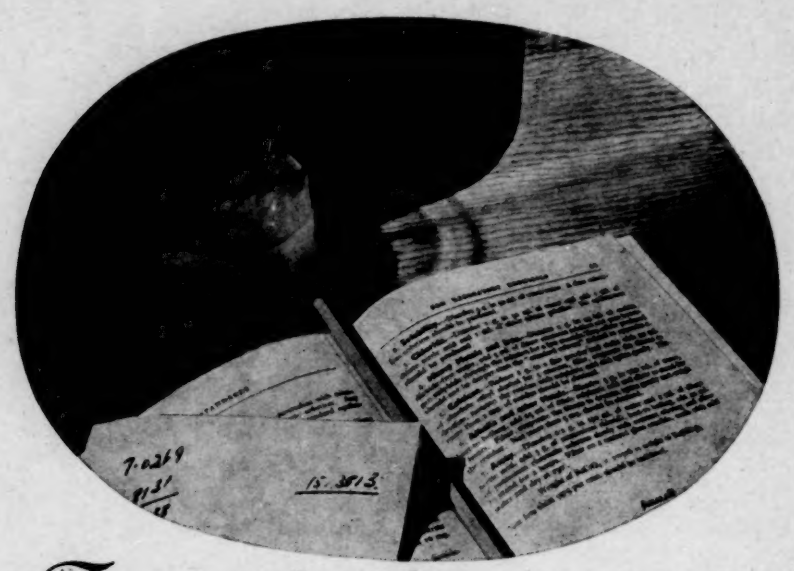

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